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TABLE OF CONTENTS FIRST PAGE

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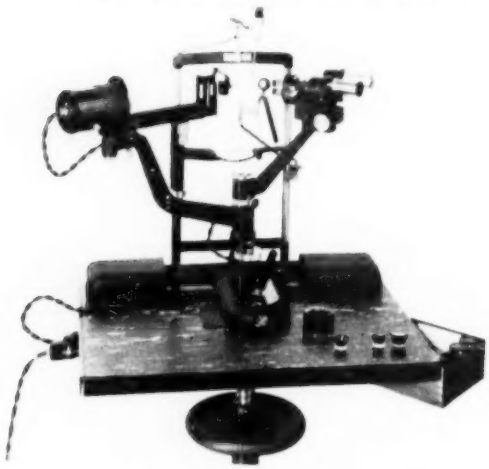

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CONTENTS

Original Articles

Goniotomy for Glaucoma Associated with Aniridia PAGE

Otto Barkan, M.D., San Francisco 1

Osteogenesis Imperfecta Congenita and Blue Sclerotics

Albert D. Ruedemann Jr., M.D., Baltimore 6

Beta-Radiation Therapy of Pterygium

J. William Rosenthal, M.D., New Orleans 17

Evaluation of Five New Cycloplegic Drugs

Bernard C. Gettes, M.D., and Irving H. Leopold, M.D., Philadelphia 24

Normal and Reversed Vision in Transplanted Eyes

L. S. Stone, Ph.D., New Haven, Conn. 28

Idiopathic Detachment of the Retina

Taylor R. Smith, M.D., and L. Harrell Pierce, M.D., Boston 36

Blepharoptosis Treated by the Friedenwald-Guyton Suture

Byron Smith, M.D., New York, and Herbert G. Pang, M.D., Honolulu, T. H. 45

Surgical Aspects of Defective Abduction

Edmund B. Spaeth, M.D., Philadelphia 49

Ophthalmological Reviews

The Electroretinogram

George W. Bounds Jr., M.D., Iowa City 63

Annual Reviews

Lids, Lacrimal Apparatus, and Conjunctiva

James H. Allen, M.D., New Orleans 90

Regular Departments

News and Comment 110

Books 116

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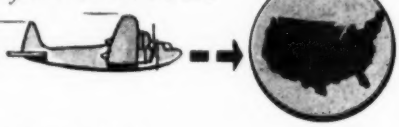

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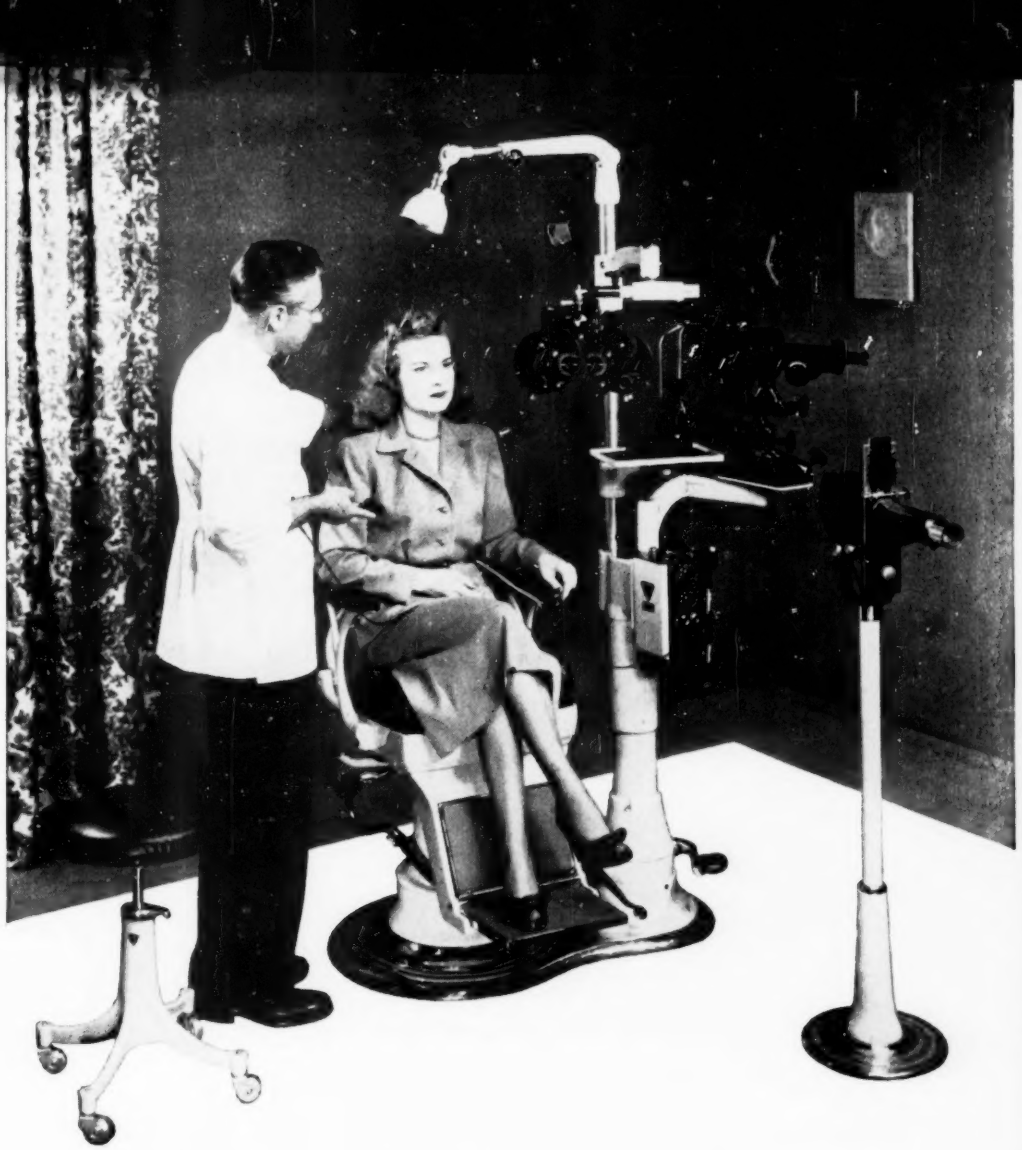

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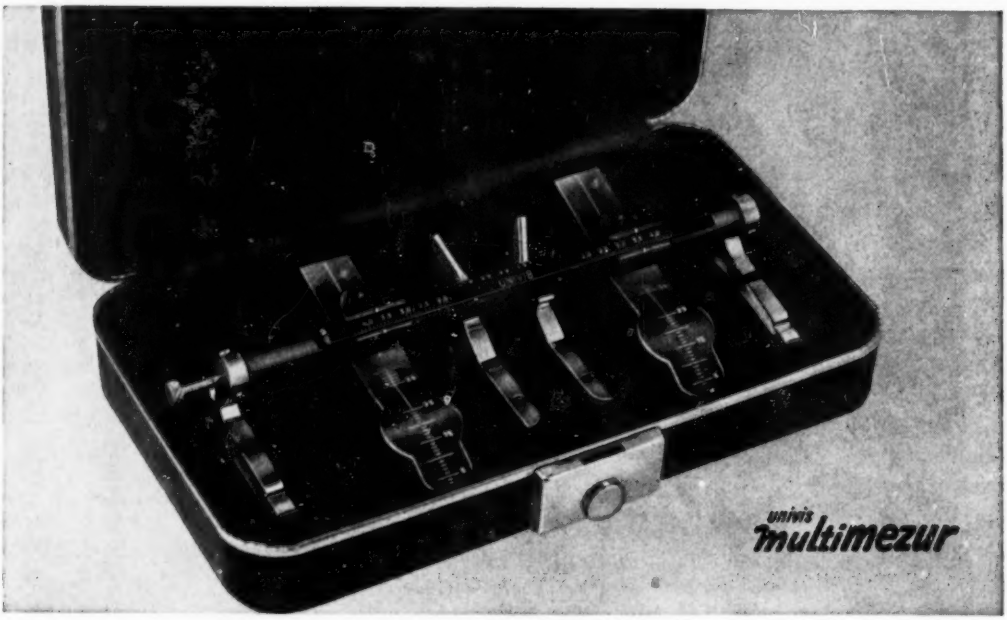

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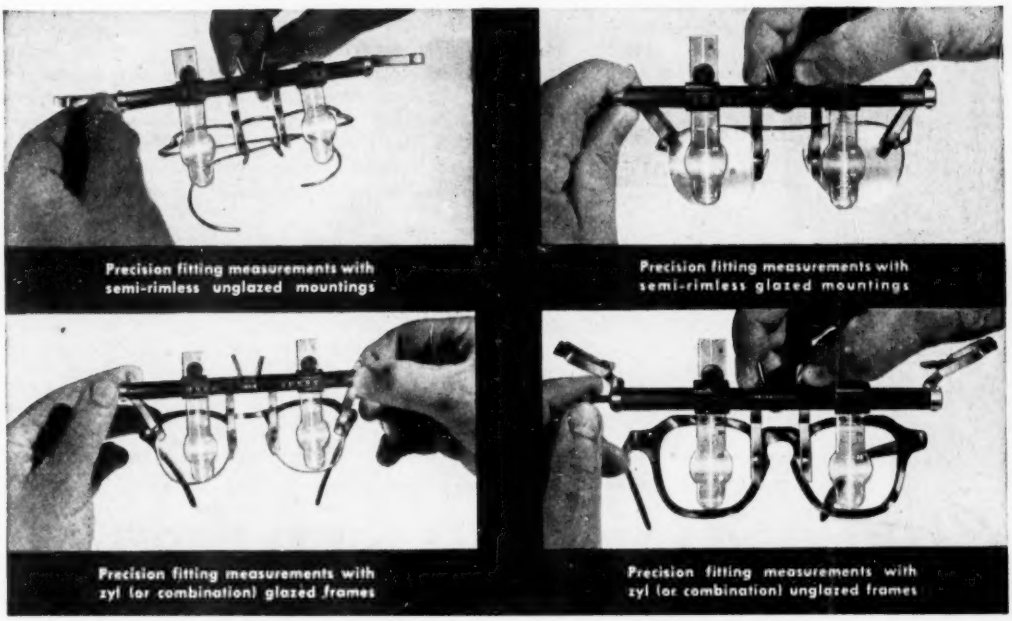
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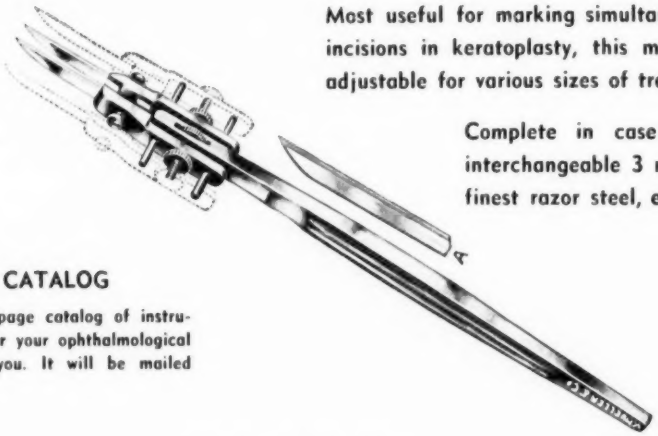

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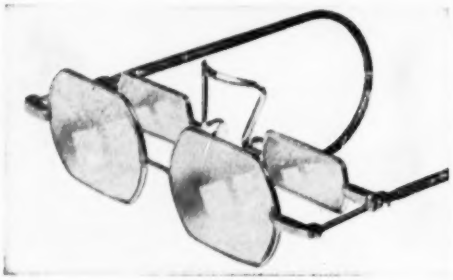

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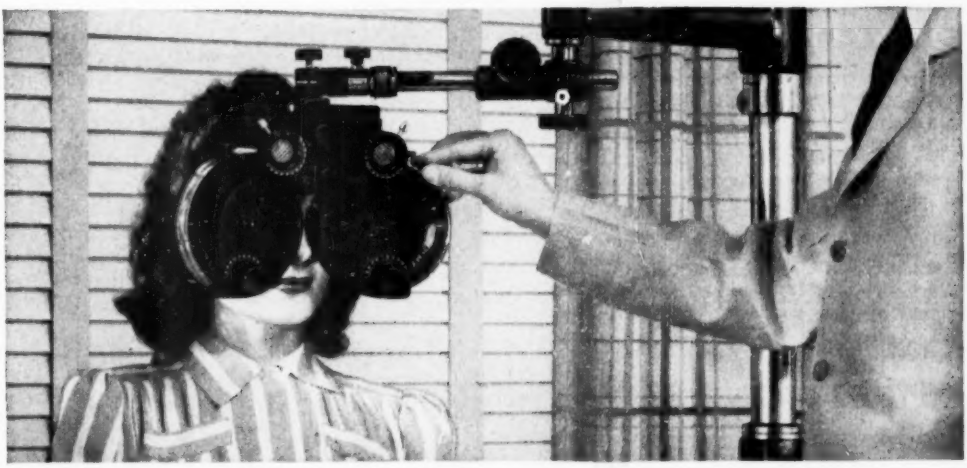

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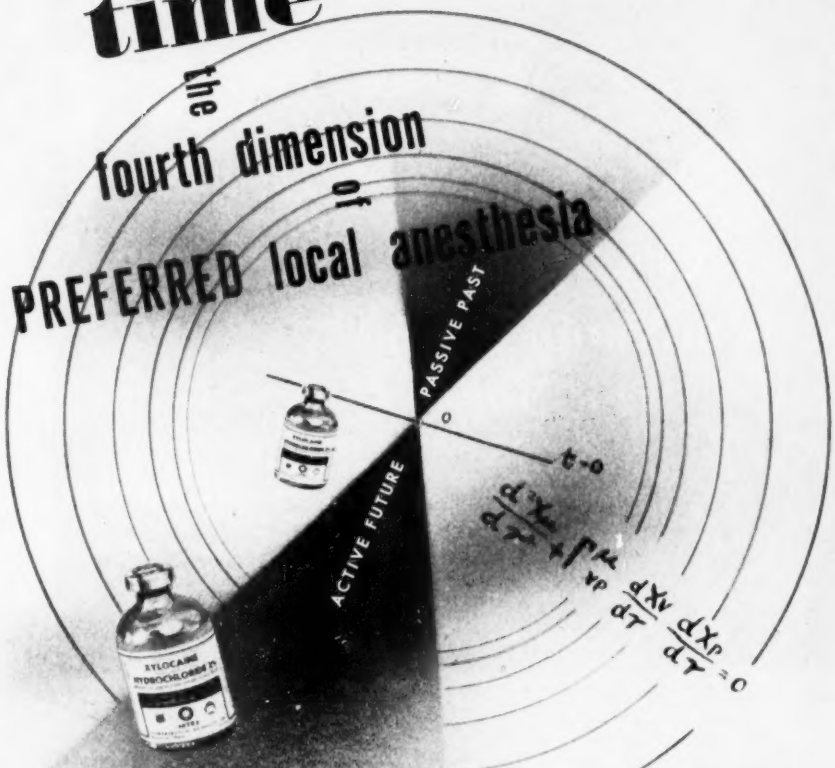

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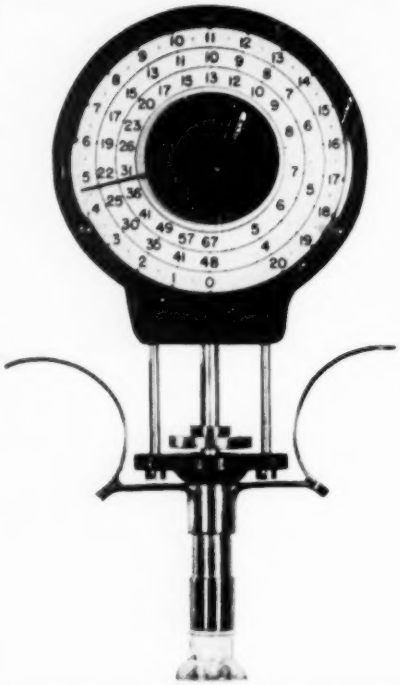

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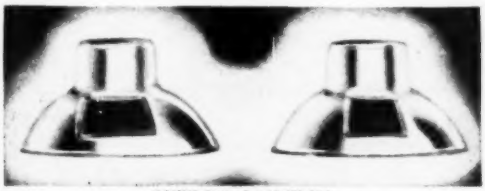

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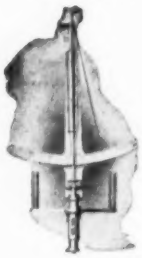

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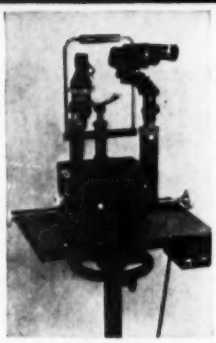

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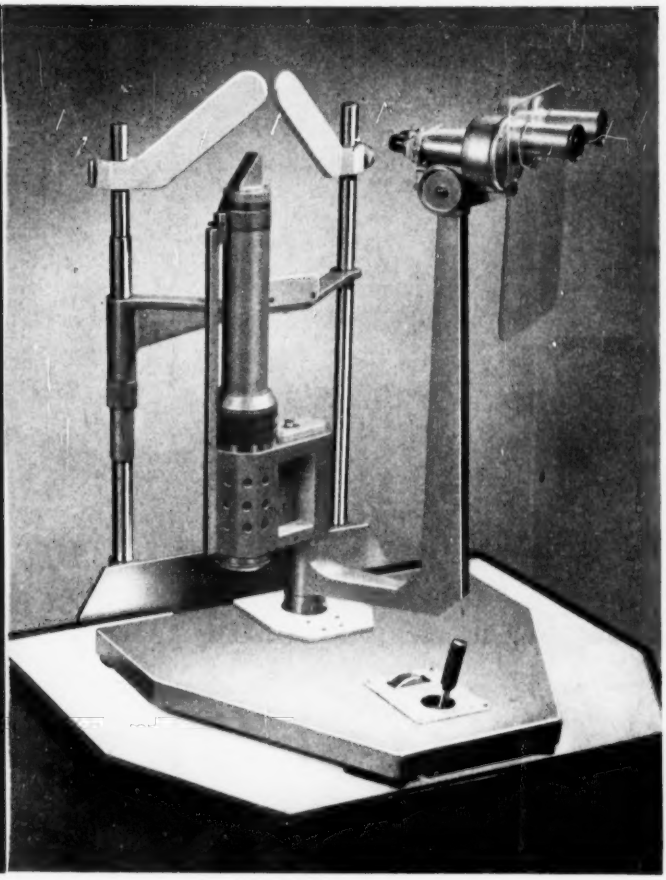

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GONIOTOMY FOR GLAUCOMA ASSOCIATED WITH ANIRIDIA

OTTO BARKAN, M.D.
SAN FRANCISCO

GLAUCOMA is often associated with aniridia (irideremia). On clinical examination the iris appears totally absent, but histologically a narrow rim of iris of varying width and some persistent mesodermal tissue in the angle have been found in all cases. In many the pigment epithelium overlaps the stump of the iris, as in an ectropion. According to Parsons,[1] the stump of iris is often adherent to the sclera at the extreme limit of the anterior chamber over a considerable portion of the circumference; part of the angle is usually open, and through this efficient filtration is maintained until some intercurrent cause leads to obliteration. It is believed that the imperfect separation of the iris from the cornea at the periphery is due to arrested development.

Recently Callahan [2] reported histologic findings in a case of aniridia with a rudimentary iris, which varied slightly in size but was about 1 mm. in length. In most of the sections the iris was in contact with the posterior surface of the cornea, forming a dense peripheral anterior synechia. Except for the small rounded tip, the iris stroma was so atrophic that it could hardly be recognized. Schlemm's canal was absent, but as the eye was blind and distended and the patient was 24 years old, this was to be expected.

Gonioscopy has confirmed the persistence of a narrow base and circular band of iris in aniridia. Troncoso [3] found the band attached at the level of the scleral trabeculum. Sugar [4] reported two cases in which a band of iris persisted through the whole circumference of the chamber angle, the latter being occupied in part by mesodermal embryonic tissue. In one of the cases there was increased pressure. François [5] examined an aniridic eye without glaucoma. It showed a narrow band of iris with an ectropionized border of the pigment epithelium, narrowing of the angle wall, and fairly large iris processes, which stopped at the level of the spur.

1. Parsons, J. H.: The Pathology of the Eye, New York, G. P. Putnam's Sons, 1906, Vol. 3 Pt. I, p. 1088.

2. Callahan, A.: Aniridia with Ectopia Lentis and Secondary Glaucoma: Genetic, Pathological, and Surgical Considerations, Am. J. Ophth. **32**:28-39 (June, Pt. 2) 1949.

3. Troncoso, M. U.: A Treatise on Gonioscopy, Philadelphia, F. A. Davis Company, 1947, p. 150.

4. Sugar, H. S., in Berliner, M. L.: Biomicroscopy of the Eye: Slit Lamp Microscopy of the Living Eye, New York, Harper & Brothers, 1943, Vol. 1.

5. François, J.: La gonioscopie dans le glaucome primitif, Ann. ocul. **181**:399-409 (July) 1948.

There appeared to be free access for aqueous to the trabeculum. He found, after assembling all the cases of aniridia mentioned in the literature, that glaucoma occurred in about 70%.

I noted a similar gonioscopic picture in two cases of aniridia without glaucoma. The first patient, P. L., a 9-month-old infant, was first seen on June 3, 1939. The iris was inserted somewhat anteriorly in a manner characteristic of typical congenital glaucoma, the abnormality being greater in the right eye than in the left. The root of the iris was slightly turned upward. The pressure was slightly increased in the right eye. The second patient, E. H., a 4-month-old infant, was seen on Jan. 23, 1951. A stump of iris was bordered by the pigment epithelium. The dark stroma was reflected anteriorly for about one-third of the breadth of the angle wall before it divided into uveal aborescences. The appearance of the trabecular zone was normal, and the tension was normal. A pink band denoting Schlemm's canal was observed. Since glaucoma may develop at a later age, an annual examination was advised in both cases.

The combined evidence of histologic examination and gonioscopy shows that in a considerable number of cases persistent uveal meshwork which is attached to the trabeculum and to the anterior surface of the iris stump pulls the latter forward and results in an adhesion of the iris stump to the angle wall up to the line of Schwalbe, thus sealing off the angle from the anterior chamber. This was the condition in the case to be reported in the present communication.

The operative prognosis in congenital aniridia has been notoriously poor. Callahan has noted the apparent inadequacy of the various types of surgery for glaucoma. In two late cases (ages 13 and 14 years) goniotomy was unsuccessful. Because of corneal haziness it was difficult to see the rudimentary iris and to locate the chamber angle. He concluded that a more basic reason for the failure of goniotomy in children of these ages was that the canal of Schlemm, if present at birth, had probably become obliterated by the long-continued increased pressure.

In the case to be reported, a goniotomy was carried out with the present simplified technique, the surgical contact glass being used, with direct visualization of the angle. The tension was normalized and has remained within normal limits to the time of report, a period of nine months. From this it may be concluded that the Schlemm-canal mechanism was present and ready to function, as it is in most cases of typical congenital glaucoma in the early stages.[6]

REPORT OF A CASE

J. C., a 4½-month-old boy, was first seen on June 8, 1951, through the courtesy of Dr. Harold Beasley, of Fort Worth, Texas, with the diagnosis of total aniridia of both eyes and congenital glaucoma of both eyes, the left eye being more affected than the right. He was born at full term after an uneventful pregnancy. His development had been normal. There was no history of blindness in the family.

Examination of Eyes.—Visual Acuity: The infant was attracted by moving objects before either eye.

External Examination: The corneal diameters, measured with calipers in the horizontal meridian, were 10.75 mm. in the right eye and 11.0 mm. in the left eye. The corneas showed cloudiness, 1+. There were no ruptures of Descemet's membrane. The right tear sac contained pus. The sac was irrigated with sulfacetimide solution, and a probe was passed.

6. Barkan, O.: Operation for Congenital Glaucoma, Am. J. Ophth. **25**:552-568 (May) 1942.

Ocular Tension: Intraocular tension was 37 mm. in the right eye and 16 mm. in the left eye (Schiøtz; 5.5-gm. weight); 23 mm. in the right eye and 12 mm. in the left eye (Schiøtz; 10-gm. weight), and 85 mm. in the right eye and 34 mm. in the left eye (McLean). No miotics had been instilled for 12 hours prior to the taking of the tension. The fundus of the left eye was normal. The right eye was not examined at this time. Dr. Beasley had found pressure increased in the left eye, but this was no longer the case at the time of my examination.

Gonioscopy: The right eye was not examined. In the left eye the angle wall was not seen in exact detail at this time. It appeared, however, that some tissue extended in a frontal plane from the epithelial pigment border of the root of the iris to the line of Schwalbe. It was decided to perform a goniotomy on the right eye after the dacryocystitis was cleared up.

Diagnosis.—The diagnosis was aniridia of both eyes, with glaucoma and chronic dacryocystitis in the right eye.

Operation and Subsequent Studies.—On June 11, 1951, with the patient under intratracheal ether anesthesia and with extra drops of 5% neostigmine bromide instilled in the right eye, tension (Schiøtz; 5.5-gm. weight) was 37 mm. in the right eye and 16 mm. in the left eye, no drops having been used in the left eye.

Goniotomy was performed on the right eye, under the surgical contact glass. Double fixation was made in the routine manner,[7] using Gifford forceps with lock, at the insertions of the superior and inferior rectus muscles, and a canthotomy was done. The epithelium was cloudy and mushy and was abraded with keratome. Thus very good visibility was afforded through the surgical contact glass, medium size.[8] Superficial stripping was done just anterior to the pigment border of the root of the iris in the nasal upper quadrant. A posterior recession of the stripped region could be observed following the blade. Only a trace of dark venous blood was noted. A moderate-sized air bubble was injected through the wound of puncture while the head was kept rotated to the side of operation in order that the air should be locked in the chamber. One drop of diisopropylfluorophosphate was given the patient while he was on the table, and 5% neostigmine bromide and diisopropylfluorophosphate were given daily thereafter. Except for the first trace, there was no blood in the anterior chamber at any time. The cornea was brilliant. The patient was dismissed on June 21.

On Sept. 11, 1951, Dr. G. L. Kilgore, of San Diego, reported a tension of 25 mm. (Schiøtz) in each eye, use of miotics having been discontinued five days previously.

On March 13, 1952, the patient was reexamined by my associate, Dr. W. J. Ferguson Jr., and me. The left eye diverged from 8 to 10 degrees. There was a fine, rapid nystagmus in both eyes. The patient, then 14 months old, was able to find small objects.

On March 14, 1952, with the use of intratracheal ether anesthesia, administration of miotics having been stopped three days previously, tension was 20 mm. in the right eye and 18 mm. in the left eye (Schiøtz; 5-gm. weight); 25 mm. in the right eye and 23 mm. in the left eye (Schiøtz; 10-gm. weight), and 32 mm. in the right eye and 30 mm. in the left eye (McLean). The corneal diameter measured 11 mm. in the right eye (margin slightly vague) and 11 mm. in the left eye. The corneas were clear and brilliant.

The optic disk in both eyes showed small, centrally placed excavations (physiological), about equal in size and depth.

Gonioscopic examination was performed with a corneal microscope (total magnification, × 25), mounted on an adjustable, movable floor stand, and a hand slit lamp.[9] Visibility was excellent. In the right eye (Fig. 1) the slightly ectropionized border of the stump of iris, which consisted of pigment epithelium, was found to be pulled up toward the line of Schwalbe by a semitransparent tissue or membrane, thus sealing the angle. The surface of this adhesion was in about a frontal plane with the line of observation. The pigment border was slightly curved in an anteroposterior direction, so that in places where the curve was concave toward

7. Barkan, O.: Technic of Goniotomy for Congenital Glaucoma, Arch. Ophth. **41**:65-82 (Jan.) 1949.

8. Barkan, O.: A New Focal Illuminator, Am. J. Ophth. **24**:439 (April) 1941.

9. Barkan.[7, 8]

the line of Schwalbe a little of the anterior stromal surface of the tag of iris was visible through the meshwork. This bit of iris looked gray and denser than the normal stroma of infants, presumably because it was fibrotic.

The goniotomy incision was begun at the 2:30 o'clock position. From this point in a direction counterclockwise to 11 o'clock the surface of the meshwork gaped, and the border of pigment epithelium had dropped posteriorly, so that it came to lie upon the ciliary processes. In the recess between it and the line of Schwalbe the angle and the angle wall appeared normal for a child the age of this infant. Slight signs of meshwork remained, but by far the major part had disappeared, leaving an appearance in the depth of normal uveal meshwork, which extended to

Fig. 1.—Angle of anterior chamber in aniridia associated with glaucoma (right eye). At the right, the rudimentary band of iris is pulled up toward the line of Schwalbe by a membrane, thus sealing the angle. At the left, the adhesion of the stump of iris has been released by goniotomy, resulting in exposure of a normal-appearing trabeculum to the aqueous. Tension was normalized.

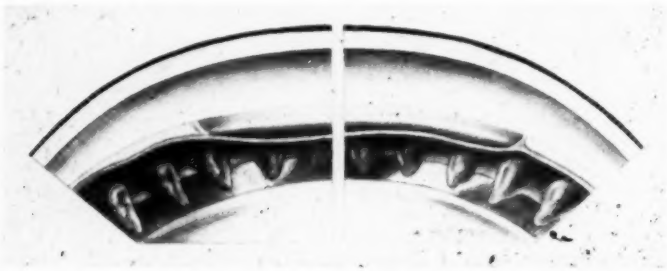

Fig. 2.—Angle of anterior chamber in aniridia (left eye). Two-thirds of the circumference of the angle is closed by the stump of iris, which is drawn up to the line of Schwalbe by a membrane of residual mesodermal tissue, thus sealing off the angle from the anterior chamber. From 1:30 to 5:30 o'clock the angle is open and the trabeculum appears normal.

the spur. Anterior to the spur the trabecular zone appeared normal. In the area of operation the pigment border was crenated, in striking contrast to the smooth, stretched appearance in the area of no operation.

There would appear to be no doubt that aqueous had been given access to the trabeculum in this region, and perhaps at either end of the stripped area to the filtration angle behind the persistent tissue. Excellent visibility permitted detailed examination of the entire stripped area, so that my associate and I feel that it can definitely be stated that there was no cleft leading to the suprachoroidal space. The incision was very superficial and had not in any place touched the angle wall itself. External drainage did not come into question.

In the left eye (Fig. 2) three-fourths of the circumference of the angle was closed by the iris stump, which was drawn up toward the line of Schwalbe by aberrant, presumably mesodermal, tissue, thus sealing off the angle from the anterior chamber. From about 1:30 to 5:30 o'clock in a clockwise direction, however, this tissue was absent, and the angle was open and normally wide, owing to the fact that the iris stump and the pigment border were not drawn up to the line of Schwalbe. A normal-appearing trabeculum could be seen in this area. The spur could be distinguished, with normal-appearing, gray uveal meshwork extending to it. The ciliary-body band was normal in appearance. But, commencing at 5:30 and running from there clockwise to 1:30 o'clock, the pigment border was attached to the line of Schwalbe and the angle was closed.

SUMMARY

In the right eye, goniotomy released the adhesion of the iris stump to the line of Schwalbe over one-fourth of the circumference. This resulted in normalization of pressure, which has been maintained without use of miotics up to the time of this report, a period of nine months.

The left eye is predisposed to glaucoma, since a large part of the circumference of the angle is closed. It appears that the portion of the angle which is open has provided sufficient outflow for the maintenance of normal tension most of the time. As a result of the extensive area of closure, there is not much threshold for regulation of the intraocular pressure, so that at a time of stress the pressure has been uncontrolled, as reported by Dr. Beasley. If the pressure in the left eye should rise at some future date, goniotomy with the contact glass would be indicated.

It would appear most likely, by analogy with the course of events in typical congenital glaucoma, that Schlemm's canal is present in most cases in the early stages, before it has become obliterated by prolonged increased pressure and by distention. On the basis of these considerations, it is important to make an early diagnosis of the glaucoma and to operate under gonioscopic control. The objective of the operation is to permit the iris stump to drop backward and open the angle.

I believe that the need for operating by direct vision with the contact glass can hardly be overemphasized, since the blade of the knife must strike a target between the line of Schwalbe and the pigment border of the iris stump, a distance of probably less than 0.5 mm. To attempt to do this blindly or by estimation from the outside without the glass, as has been suggested because of the supposed difficulty of operating with the glass, does not appear justified when it is considered that there is a lifetime of vision at stake. The technique of operating under gonioscopic control with the glass, once learned, is simple. A description of the simplified technique is being published.

CONCLUSIONS

The developmental anomaly in the angle which is the cause of glaucoma in aniridia appears to be similar to that which is the cause of typical congenital glaucoma. Residual embryonic tissue in the angle is a common finding in aniridia. Glaucoma results in those cases in which this tissue pulls the rudimentary root of the iris toward the line of Schwalbe, thus sealing off the angle from the chamber. In the present paper, the first successful goniotomy in a case of glaucoma associated with aniridia is reported. Tension has been normalized without miotics for nine months by opening the angle and exposing the trabeculum to aqueous over one-fourth of its circumference. It is suggested that early goniotomy, under gonioscopic control, is indicated in cases of glaucoma associated with aniridia.

OSTEOGENESIS IMPERFECTA CONGENITA AND BLUE SCLEROTICS

A Clinicopathologic Study

ALBERT D. RUEDEMANN Jr., M.D.
BALTIMORE

OSTEOGENESIS imperfecta congenita (Vrolik) is usually a hereditary disease. It is characterized by fragility of bones, so-called blue sclerae, otosclerosis and deafness, relaxation of ligaments and skeletal muscles, dental defects, and other deficiencies related to mesodermal tissues. It is known variously by such names as Lobstein's syndrome, osteopsathyrosis idiopathica, and van der Hoeve's disease.

HISTORICAL REVIEW

Ekmann, in 1788, carefully described the disease in three generations of patients. He did not mention blue sclerae and deafness. Subsequent to this report cases of multiple fractures were described by Lobstein, Vrolik, and others. Thin sclerae were described by Henzschel,[1] in 1831, in a female with aniridia. Gescheidt,[2] in 1832, described blue sclerae in a case of microphthalmos. Neither author noted a familial tendency or other associated characteristics of the disease. In 1841 von Ammon,[3] without the aid of magnification, noted the thinness of the sclera in dissected eyes and implied that a blue appearance was due to increased transparency. He appreciated that this condition was characteristic of the fetal eye. Cornaz,[4] in 1848, and others, noted transparent sclerae as an isolated phenomenon. A full 50 years passed, however, before Spurway,[5] in 1896, related blue sclerae to hereditary fragility of bones. He described a child of 4 years who had sustained multiple fractures and who had a family history of the same condition extending back four generations. Various members of the child's family had a bluish tinge to the eyeballs. Four years later Eddowes [6] described blue sclerotics and broken bones in two patients and ascribed both to a want of quality or quantity of fibrous tissue.

From the Wilmer Ophthalmological Institute, Johns Hopkins Medical Center.

1. Henzschel: Ztschr. Ophth. **1**:52, 54, 1831.

2. Gescheidt, A.: Über Microphthalmos: ein Beitrag zur Lehre von den Bildungsfehlern des Auges, Ztschr. Ophth. **2**:257, 1832.

3. von Ammon, F. A.: Klinische Dartstellungen der Krankheiten und Bildungsfehler des menschlichen Auges der Augenlider und der Thränenwerkzeuge, Berlin, 1841, p. 73.

4. Cornaz, C. A.: Des abnormités congénitales des yeux et de leurs annexes, G. Bridel, Lausanne, 1848, p. 67.

5. Spurway, J.: Hereditary Tendency to Fracture, Brit. M. J. **2**:844, 1896.

6. Eddowes, A.: Dark Sclerotics and Fragilitas Ossium, Brit. M. J. **2**:222, 1900.

The general clinical picture has been carefully described in the excellent monographs of Bell,[7] covering 73 families and 463 cases, and Seedorff,[8] covering 55 families with 180 affected members.

Studies in relation to the pathology of this disease have been limited mainly to the changes found in osseous tissues. A review of the literature revealed but three cases investigated in regard to the pathologic changes in the eye.

Buchanan,[9] in 1903, studied the eye of a 9-year-old white girl whose eye required enucleation because of an injury. Blue sclerotics were a family trait, but bony defects were not noted in the child or her family. Ophthalmologic examination revealed myopia and conical cornea. Grossly, the choroid was seen through a sclera of estimated one-third normal thickness, while the cornea was three-fifths normal thickness. On histologic examination, Buchanan noted a diminished number of scleral fibers and cells, though he felt the distribution of fibers was normal. He found the cornea similarly defective, with an absence of Bowman's membrane. Later observers found Bowman's membrane present but thinner than normal.[10]

Bronson,[11] in 1908, examined the eye of a baby boy who died of pneumonia at 11 months of age. The infant seemed to be developing normally. There was no history of fractures, but he did have gray-blue sclerae. The family consisted of 55 members, 21 of whom had blue sclerotics. Of these 21 members, 13 had fractures; 6 died in infancy without fractures, and an infant and another child, aged 6 years, had no fractures. A complete autopsy was not performed, but one eye was examined by Dr. J. V. Patterson, ophthalmologist to the Royal Infirmary, Edinburgh. He stated that the sclera was of normal thickness and that the number of fibers was normal for a child of that age. In his opinion the blue sclerae were due to increased translucency.

In 1934 Casanovas [12] noted thin sclerae and pronounced uveal pigmentation in a 9-month-old boy with no family history but a suggestive clinical picture.

PRESENT STUDY

The present study consists of three cases of osteogenesis imperfecta diagnosed either clinically or pathologically. Two eyes were obtained at autopsy, and the third was enucleated for clinical reasons. The first eye was that of a premature newborn infant; the second, that of a full-term newborn infant, and the third, that of an adult. It is the purpose of this paper to report the ocular pathology in this disease. The method used was as follows:

Technique.—1. The eyes were fixed in Bouin's solution and embedded in paraffin. Sections were stained with hematoxylin and eosin and by the Mallory, Verhoeff-Van Gieson, periodic acid-fuchsin, and thionine techniques.

At the suggestion of Dr. R. H. Follis, associate professor of pathology in The Johns Hopkins University School of Medicine, a silver stain for reticulum, namely, the Gomori [13] modification of the Bielschowsky-Maresch method, was used. With this technique reticulum stains black, owing to its specific ability to fix colloidal silver, and collagen is stained red. Actually, the

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11. Bronson, E.: On Fragilitas Ossium and Its Association with Blue Sclerotics and Otosclerosis, Edinburgh, N. J. **18**:240, 1917.

12. Casanovas, J.: Blue Scleras and Fragilitas Ossium, Arch. oftal. Hispano-am. **34**:133, 1934; abstracted, Am. J. Dis. Child. **50**:1298, 1935.

13. Gomori, G.: Silver Impregnation of Reticulum in Paraffin Sections, Am. J. Path. **13**:993, 1937.

transition from black to red is due to the intensity of the stain. As reticular fibers form into mature collagen bundles, a red color is observed. With this technique, characteristic changes were noted in all three cases.

2. Each abnormal eye was then compared with a normal eye in a supposedly similar developmental stage. The infants were judged according to weight,[14] and the adult, as to age, sex, and color.[14]

3. Sections of each eye were stained at the same time, under similar conditions, using the Gomori, Verhoeff-Van Gieson, and Hotchkiss techniques. The Verhoeff-Van Gieson method was used in an attempt to determine possible abnormalities of elastic tissue in this disease.

In the following case reports the findings with the silver stain will be given in detail. The findings with other stains will be summarized below.

CASE 1.—A white boy, weighing 1,035 gm., delivered at Philadelphia Naval Hospital, died several hours after birth. The left eye was sent for study to the pathology laboratory of the Wilmer Ophthalmological Institute. The family history was noncontributory. There is one child, born prematurely one year prior to this one, and considered normal. The prominent physical characteristics seen at autopsy were multiple fractures and so-called blue sclerotics. Grossly, the eyes appeared otherwise normal. The skull cap consisted mainly of membranous tissue with only a suggestion of calcification. There were multiple fractures of the parietal bones and a large subarachnoid hemorrhage in the right occipital area. Every long bone was fractured in one or more places, and there were fractures in the rib cage and vertebrae. Osseous-like nodules were noted on the pleural surface. The lungs were atelectatic.

The general histologic structure, with the exception of the bones, was not unusual.

Ocular Pathologic Findings.—Figure 1*A* shows a section of sclera taken from the normal eye of a stillborn infant weighing 1,020 gm. No abnormality was found in this eye. Collagen bundles were well formed and compact. Longitudinal bundles were already formed and took a red color with the silver stain. Reticulum fibers were extremely rare.

Figure 1*B* shows a section of sclera taken from a similar position in the eye in Case 1. Reticulum fibers were occasionally seen, and, although this eye was at least as mature as the normal one with which it was compared, there was not nearly as much collagenous tissue.

Corneal tissue from the normal eye (Fig. 2*A*) presented an interesting contrast to that from the dysplastic eye. The fibers of the stroma were well formed into more or less mature collagen bundles. In the abnormal cornea (Fig. 2*B*) there was deficiency of the stromal fiber bundles, with an occasional reticular fiber, while the epithelium, Bowman's membrane, Descemet's membrane, and endothelium were readily seen. There may have been some thinning of both sclera and cornea as compared with the normal. Examination of the uveal tract and retina revealed no abnormality.

CASE 2.—A Negro girl, weighing 1,400 gm., was spontaneously delivered after prolonged labor (44 hours), presumably near term. (Evidence of uterine inertia and premature separation of membranes was noted. The duration of pregnancy was 39 weeks, or 276 days.) The mother was in good health, and pregnancy was uncomplicated. The child was in poor condition when delivered and died after 27 minutes of life.

The family history, through both maternal and paternal grandparents, was noncontributory. The father, aged 30, sustained fractures of both legs when a truck tire blew up, throwing the rim against his legs. There was no other history of fractures. Ophthalmologic examination of the father, made at home, showed nothing abnormal. Ophthalmologic examination of the mother revealed an entirely normal condition. She had never sustained a fracture.

14. A comparison of infants based on weight alone is inadequate, since the underdeveloped bone structure in the baby with osteogenesis imperfecta places the child in a more immature weight group. Comparisons of viscera, bone-maturation areas, retina, gestation periods, etc., revealed that this was actually the case. However, crown-heel, crown-rump values were also unsatisfactory. Actually, in terms of this study, the immaturity of the normal infant specimens only serves to emphasize the differences observed. In the second case the abnormal eye was compared with the normal eye of a full-term baby, and the differences were more striking.

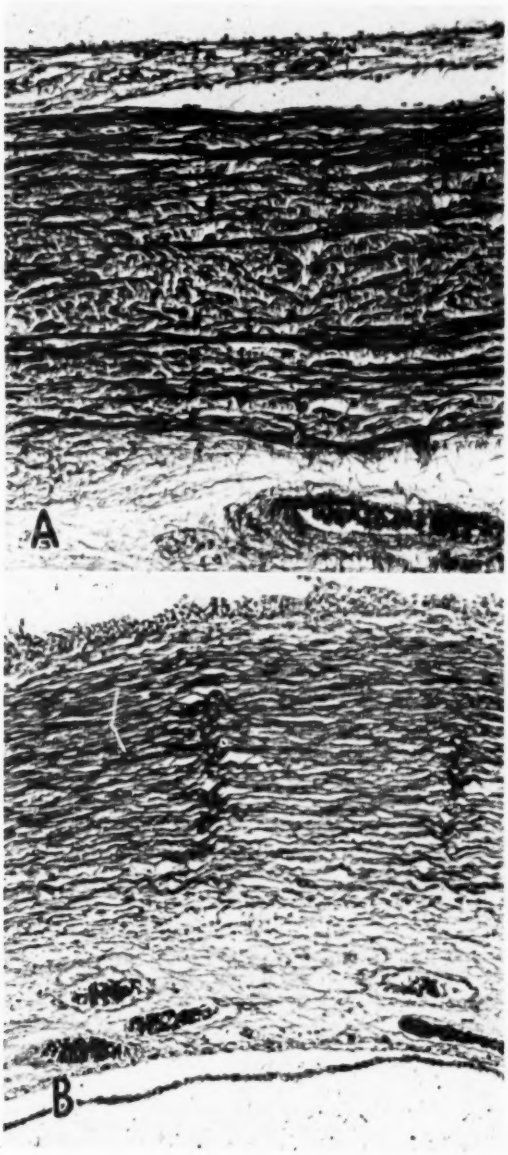

Fig. 1.—*A*, section of sclera taken from the eye of a 1,020-gm. stillborn infant. *B*, section of sclera taken from the eye of a 1,035-gm. premature infant. Silver stain; × 140.

There are three other siblings. The oldest, aged 17, had a different father. He was said to be entirely normal, with white sclerae and no history of fracture. A boy, aged 2 years 3 months, had normal eyes. He had had no fractures. A blood brother, born after the death of this child and 3 months old at the time of this report, was in excellent health, and his eyes were normal.

The general pathologic picture will be reported elsewhere by Dr. Follis, who considers this case the only one of true osteogenesis imperfecta congenita encountered in over 23,000 autopsies

Fig. 2.—*A*, section of cornea taken from the normal control. *B*, section of cornea from the eye of the baby with osteogenesis imperfecta. Silver stain; × 140.

at the Johns Hopkins Hospital. His studies have revealed changes in the skin and bones hitherto unreported.

Ocular Pathologic Findings.—Figure 3.*A* is a section of sclera from the normal eye of a stillborn infant weighing 1,360 gm., and *B*, a section of sclera from an eye of the affected infant. The areas illustrated are from similar positions near the optic nerve. The generally normal pattern of collagen bundles was seen in the sclera of the uninvolved eye, while the sclera of the abnormal eye showed persistence of reticulum with underdevelopment of collagen bundles. The fibrous coat was markedly thinner in the abnormal eye.

The corneal changes were essentially the same as in the first case (Fig. 4). The normal control had a regular collagen-bundle stroma with rare reticular fibers; while the abnormal cornea was extremely thin, there were many reticular fibers and relatively little collagen. All the corneal layers were noted. The retina and uveal tract appeared essentially normal. When the

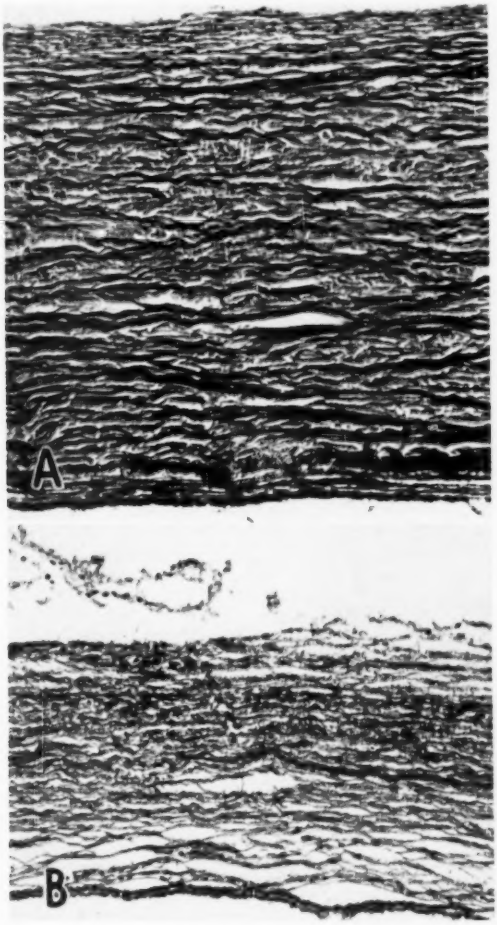

Fig. 3.—*A*, section of sclera taken from the eye of a 1,360-gm. stillborn infant. *B*, section of sclera taken from the eye of a 1,400-gm. baby with osteogenesis imperfecta. Silver stain; × 140.

sections of the two corneas are placed side by side, the marked differences in structure are revealed.

Case 3.—A Negro woman aged 36 had been followed since 1947 in the outpatient department of the Wilmer Ophthalmological Institute. The patient was an adopted child, and her family history was therefore unknown. The past history was marked by fractures. As a baby her left leg was broken twice—at the ankle and at the hip. At the age of 9 years she sustained a compound fracture of the right tibia and fibula. Somewhat later the right elbow and the little finger

of the left hand were fractured. Both were set, with resulting deformity. In 1943 a fall resulted in the fracture of two ribs. Since prior to 1929 the patient had presented prominent scoliosis. She stated that in none of the accidents mentioned was any particular pain involved. She had sustained no sprains or dislocations and had no hearing difficulties.

In 1947 a general medical work-up revealed no evidence of endocrine imbalance, and repeated estimates of serum calcium and phosphorous were within normal limits. Alkaline phosphatase activity of the serum was also normal.

The patient's history bore out the correlation of the disease with defective teeth. She has had 10 extractions of permanent teeth because of caries, and in April, 1951, the extraction of a

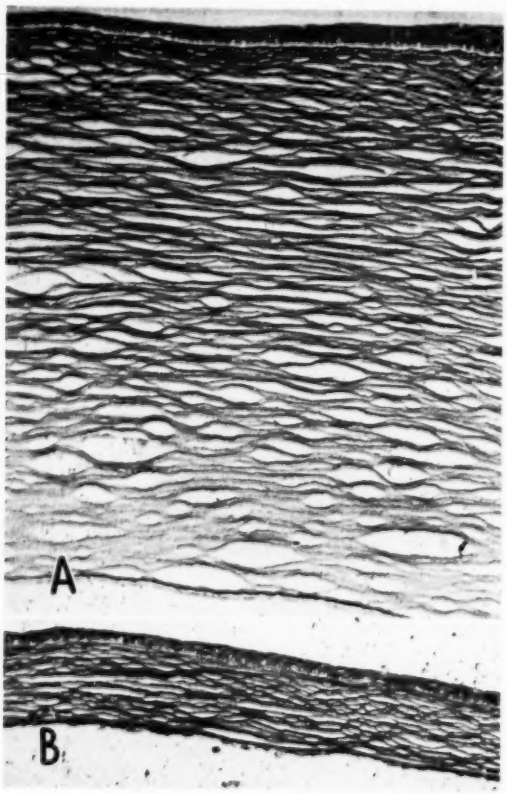

Fig. 4.—*A*, section of cornea taken from the normal control. *B*, section of cornea taken from the abnormal eye. Silver stain; × 140.

carious third upper molar was complicated by fracture of the maxillary tuberosity. The tooth could not be dissected from bone, and the entire mass had to be removed. Healing was satisfactory, without antral defect, and was not complicated by severe pain.

The patient had thin skin, and though she had had many cuts, the wounds healed rapidly, with little scarring. A biopsy specimen of skin was taken for study, and the wound thus created was nearly healed in less than 40 hours. Histologic changes were similar to those found in the second case and will be presented by Dr. Follis.

The ophthalmologic history is interesting. When examined in 1947 the right eye was phthisical; there was no light perception. The patient stated that she had been blind in this eye

Fig. 5.—*A*, section of sclera taken from the eye of a 36-year-old Negro woman. *B*, section of sclera taken from the eye of a 36-year-old Negro woman with osteogenesis imperfecta. Silver stain; × 140.

for at least 17 years. There was deep-angle glaucoma of the left eye; vision was 20/20. So-called blue sclerae were noted, and the patient stated that this condition had been present as long as she could remember. After her first visit she had required trephination of the left eye for control of the glaucoma, and the right eye had been enucleated because of pain.

Fig. 6.—*A*, section of cornea taken from the eye of a 36-year-old Negro woman enucleated because of phthisis bulbi. *B*, section of cornea taken from the eye of the woman with osteogenesis. Silver stain; × 140.

Microscopically, the characteristic picture of phthisis bulbi was noted in the right eye. The silver-impregnation technique revealed abnormalities similar to those found in the first two cases. As a control, an eye from a Negro woman aged 36 who died during anesthesia was compared with the eye in the case of osteogenesis imperfecta. The generally normal collagen bundles in

the sclera were noted. The abnormal sclera, however, showed a striking deficiency of collagen tissue with retention of reticular fibrils. The essential differences are revealed by placing the two sections side by side (Fig. 5*A* and *B*).

Figure 6*A* shows the cornea of the eye of a Negro woman aged 36 which had been enucleated because of post-traumatic phthisis bulbi. The configuration of stromal bundles is relatively normal. (The sclera was also normal.) In comparison, the section from the abnormal case (Fig. 5 *B*) reveals retention of reticular tissue with striking reduction of collagen fiber bundles.

The results of the application of other stains to sections of all three eyes are summarized as follows:

Hematoxylin-and-eosin-stained sections showed obvious thinning of the sclera and cornea, as compared with controls. In the first and third cases this was evident only upon comparison with the normal counterpart. However, no pronounced abnormality in the fibrous structures was recognizable. The Verhoeff-Van Gieson technique revealed the presence of elastic fibers in the sclera in approximately normal abundance. The periodic acid-fuchsin technique gave a generally denser stain of the sclera and cornea of the abnormal eyes than of the control eyes. The other staining techniques revealed some variations in the fibrous tissues, but no conclusion could be drawn.

COMMENT

Several interesting points may be raised in connection with the three cases shown.

1. Since the discovery of Mall,[15] in 1891, of a new type of connective tissue, which he called reticular, or lattice, fibers, there has been much controversy over the nature of this substance. Maresch,[16] in 1905, noted the specific argyrophilic effect of reticulum, using the Bielschowsky silver-impregnation technique. Since then, chemical studies have generally indicated that reticulum is a protein complex, closely related to collagen and rendered prominent in tissues by a silver stain.[17] Examinations with the electron microscope have revealed a similar structure for reticulum and collagen.[18]

Several factors lead many observers to believe that reticulum is actually a precollagenous tissue: (*a*) Argyrophilic networks were the first to appear in the formation of collagen tissues and were probably an immature stage of collagen fibers. (*b*) Reticular fibers were most numerous in relation to undifferentiated mesenchymal tissues. (*c*) The proportion of reticulum to collagen was greater in young than in adult animals.

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16. Maresch, R.: Über Gitterfasern der Leber und die Verwendbarkeit der Methode Bielschofskys zur Darstellung feinster Bindegewebsfibrillen, Centrabl. allg. Path. u. path. Anat. **16**:641, 1905.

17. Nageotte, J., and Guyon, L.: Reticulin, Am. J. Path. **6**:631, 1930. Mallory, F. B., and Parker, F., Jr.: Reticulum, Am. J. Path. **3**:515, 1927. Reticulin, in McLaughlin, G. E., and Theis, E. R.: Chemistry of Leather Manufacture, New York, Reinhold Publishing Corporation, 1945, Chap. 3, pp. 41-42.

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2. Structural defects, indicated by hydrophthalmos,[3] megalocornea,[19] keratoconus,[20] and myopia,[7] have been pointed out by other observers in cases of blue sclerotics. The eyes in Case 2 appeared larger than those of control eyes of infants of the same age. The patient in Case 3 had juvenile glaucoma. The possible relation of these structural defects to the collagen deficiencies should be considered.

3. The blue appearance of the eyeball is due to the scleral transparency. This may be due to several factors: (*a*) The fibrous coats are thinner. (*b*) The deficiency of collagen bundles and generally fewer fibers in a looser framework may reduce scattering of light. (*c*) The increased density of staining with the periodic acid-fuchsin technique suggests the possibility of a relative increase in the mucoid component of the tissue. The term blue sclerotics is obviously a misnomer—clear sclerotics is more indicative of the true histologic character of this tissue.

4. The possible relation of this disease to endocrine imbalance is not indicated by this series. The two infants had essentially normal endocrine systems. Parathyroid hyperplasia, as noted by Bauer [21] and Dietrich,[22] was not noted in either infant. The adult studied had no evidence of endocrine abnormality.

5. Hereditary factors were not brought out in this series. In two of the three cases the family history was negative for the condition. It is well known that this disease may have a sporadic incidence.

6. The abnormalities in the fibrous coats of the eye, specifically, the corneal stroma and sclera, would appear to be similar to the changes in the bone and skin, namely, deficiency in collagen formation. Further studies, relative to teeth, muscle, blood vessels, etc., are needed to prove a generalized involvement of so-called mesenchymal tissues.

SUMMARY

Three eyes obtained from persons having osteogenesis imperfecta congenita are compared with their normal counterparts.

A general deficiency of collagen and retention of the immature precollagenous reticulum fibers were noted. This deficiency varied in severity in different cases. Scleral transparency appeared to be due to this collagen deficiency. The uveal tract and retina appeared normal except in the third case, in which complicating factors were present. A study of elastic fibers with the Verhoeff-Van Gieson technique has so far revealed no deficiency of elastic tissue as compared with the normal. The collagen bundles in the cases of osteogenesis imperfecta took a generally denser stain with the periodic acid-fuchsin technique. This may have been due to an increase in the mucopolysaccharide ground substance, indicating an immature fibrous tissue.

Dr. R. H. Follis and Dr. Jonas Friedenwald assisted in this study. Miss Coffee, Miss Rogus, and Mr. Parker prepared slides and photographs.

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BETA-RADIATION THERAPY OF PTERYGIUM

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NEW ORLEANS

THE PRESENT study has three objectives: (1) to evaluate the usefulness of beta-irradiation from a radium D applicator in the therapy (*a*) of primary pterygium and (*b*) of recurrent pterygium; (2) to find an effectual and useful dosage schedule in this therapy, and (3) to compare the effectiveness of radium D with that of surgery alone and with that of combined surgery and x-irradiation in the treatment of primary and recurrent pterygium.

MATERIAL AND METHODS

Included in this study were 77 patients, with a total of 85 eyes with pterygium. Thirty-six patients, and 42 eyes, were treated surgically. Forty-one patients, and 43 eyes, were treated with beta-irradiation. Since some patients in the surgical group had recurrences, several were treated for recurrent pterygium. This does not mean, however, that several of the patients with recurrent pterygium did not have one or more secondary surgical procedures in an attempt to eradicate the recurrent growth.

All patients were operated on and treated in the clinics, wards, and operating rooms of Charity Hospital of Louisiana, New Orleans. All operations, radium treatments, and other therapy were carried out by me.

For all patients in the radium-D-treated group Swanberg's 10-mc. applicator [1] was used, as described and pictured in Figure 1.

The following routine was used in treating the patients with radium D. Therapy was carried out in the eye clinic of Charity Hospital of Louisiana. A nurse applied one drop of 0.5% tetracaine hydrochloride to each eye, followed by another drop in the involved eye (only) in two minutes and a third drop in the involved eye five minutes later. The patient was then placed supine on a treatment table, while I checked the chart for the dosage time and the eye to be treated. After separating the lids with my fingers, I placed and held the flat end of the applicator on the place on the involved eye to be treated. The lids were then released. Time was noted on the minute and second hands of my watch. When the appropriate time had elapsed, the applicator was removed from the eye, sterilized, and put back into its case. Records of the procedure were kept on a work sheet and on the patient's hospital chart.

Although its use is recommended by some authors, I did not employ a lid speculum. It was necessary to separate the patient's lids much less by having the applicator hold them open, and the subjective fear of treatment was lessened, since (1) the procedure appears to be a simpler one without the use of a speculum, (2) there is no tension on the lids to cause reflex blepharospasm, and (3) the patient's eye seems to be more under his control and less in the hands of the physician. Of course, some patients will squeeze the lids against the applicator at

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This work was originally submitted as a thesis to the faculty of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfillment of the requirements for the degree of Master of Medical Science (M.Sc. [Med.]) for graduate work in ophthalmology.

1. Swanberg, H.: A New Ophthalmologic Applicator for Pure Beta Irradiation Utilizing Radium D, Mississippi Valley M. J. **70**:71, 1948.

first and roll their eyes around, but if assured they soon become used to the sensation and cooperate. The opposite eye was also tetracainized to eliminate reflex blinking from that source.

Treatments were of the contact type, but usually more than one area was covered during each treatment.

Fig. 1.—Swanberg radium D ophthalmic applicator.

It is a circular plaque attached to a rod and handle and is devised for pure beta-irradiation. The treatment surface is 9 mm. wide, with a 5.6 mm. radioactive diameter, and when 10 mc. of radium D is incorporated, it contains eight times the amount of radioactive material per square millimeter of surface area as does a full-strength, radium-element plaque. The treatment surface has an 0.05 mm. aluminum face (filter), which has a density about one-sixth that of 0.1 mm. monel® metal, the filter used on radium-element plaques, thus greatly increasing the effective beta-ray output. From Swanberg,[1] by permission.

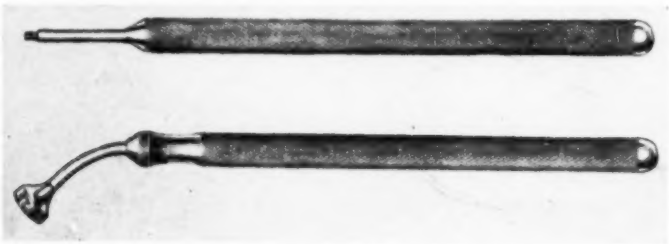

Fig. 2.—Views of the improved Swanberg applicator.

It has been reported that the patient will tire of a treatment that lasts as long as 5 to 10 minutes, as these did. Quite on the contrary, I found that the patients, being recumbent, could easily remain still for the necessary time.

The only reaction to treatment noted in these patients was that of conjunctival hyperemia. This was noticed as soon as the applicator was removed from the eye and was probably an active hyperemia, coming partly from irritation due to the tetracaine and partly from mechanical stroking of the conjunctiva by the applicator.

OPERATIVE CASES

Of the patients treated surgically, 13 were males and 23 females; 19 were white patients and 17 Negroes. The ages ranged from 14 to 81 years, with an average of 50.3 years. The majority of these persons had lived more or less an outdoor life. Patients who were listed as having no occupation were for the most part living on pensions of various sorts. Many of them had done manual outside labor for years before their retirement.

Only three patients had undergone previous therapy for pterygium. These pterygia were all recurrences following the McReynolds transplantation; in one case the grafting had been done three times previously. In all these cases recurrence was the result.

All the pterygia but two were medial. The only complication encountered was actually postoperative, being conjunctivitis, which was successfully treated. There was no untoward occurrence during the procedures.

Various local and general incidental conditions occurred with these pterygia. None had any bearing on the course of the pterygium.

In 33 cases the McReynolds technique was employed; in 9, the Blaskovics technique, and in 1, the Hobby technique. Of the group in which the McReynolds technique was employed, the lesion recurred in five (15.2%); of the group in which the Blaskovics technique was used, the lesion recurred in five (55.5%), and in the one case in which the Hobby operation was done there was recurrence. All three recurrent pterygiums had been operated on previously by the McReynolds technique; of these, the Blaskovics procedure was used in two, in both of which there was recurrence, and in one another McReynolds procedure was carried out, with recurrence.

For this work, a case was judged to be one of recurrence if there were any vessels which grew onto the corneal scar from the previous operative site. I followed several of these early recurrences and noted that soon connective tissue and more vessels followed the original small capillaries until a full pterygium had been formed—a mature recurrence.

Only one pterygium recurred in this series after an apparent cure of 3½ months, and that was after 8 months. The exact time of recurrence in this case, however, could not be determined because the patient did not return for regular examinations. It is the conclusion from this group of cases, therefore, that if no sign of recurrence appears within three to four months of the operation for pterygium a cure may be considered to have been effected.

By this criterion, 10 of the "cures" by the McReynolds method and 1 of the "cures" by the Blaskovics technique should be omitted from consideration in this series.

EYES TREATED WITH RADIUM D

In this series of 41 cases, 46 eyes were treated. Fifteen patients were males and 26 females; 16 were white persons and 25 Negroes. Their ages ranged from 9 to 79 years, with an average of 53.5 years. Twenty-seven pterygia were primary; 13 were recurrent, and 3 were pseudopterygia.

Information was obtained from most patients concerning the length of time the pterygium had been present before therapy was begun. From the variable answers (1 month to 20 years) and the appearance of the growths, it was evident that this information was not reliable. Such data, even if relatively accurate, would be only an estimate on the part of the patient.

The occupations of 36 of the 41 patients were recorded; only 5 were doing work of an inside type, where they were not exposed to the elements. Three of these patients, however, had previously done outside work. Such findings tie in with those of the operative group and with the findings of other authors.

Treatment with beta rays of radium produced only minor complications. Two patients reported that their eyes remained red for three days after each treatment. No symptoms were produced. No other reactions or complaints were noted.

Each patient received individual doses of radium of either 5 or 10 minutes' duration. Fifteen eyes received the 10-minute dose, and in all but three of these the irradiations were done at intervals of one month. The remaining three eyes received treatments at two-week intervals. Twenty-eight eyes received five-minute doses, and these treatments were given weekly to 20, every two weeks to 4, every three weeks to 1, and monthly to 2 eyes.

For the eyes receiving 10-minute doses a series of four treatments was usually prescribed. Two of the 15 eyes got only three treatments, and 1 got five treatments.

For the eyes receiving five-minute doses a series of six applications was usually prescribed. However, of these 28 eyes, 1 received one application (uncompleted case); 1 each received two, three, five, and eight applications; 7 received four applications, and 16 received six applications.

Although these dosage schedules may seem somewhat haphazard, they are not, as evidenced by the cures obtained in Cases 2 and 13. The answer lies in the relation of the total therapy (in millicurie-hours) obtained to the type of pterygium treated. In general, the flatter and less vascular growths take less total therapy for a cure than the meaty, succulent, more vascular pterygia. Therapy in pseudopterygia should be judged also with attention to the etiologic factor in the condition and the extent of pathological changes present. A total treatment dose of 2.50 mc.-hr. should be sufficient to cure a flat type of growth, while 5 to 6.50 mc.-hr. should be applied to the thicker, meatier pterygia.

Tabulation of the total therapy received by these 43 eyes shows that 18 eyes received 5.00 mc. hr.; 13 eyes, 6.66 mc. hr., and 7, 3.33 mc. hr. One eye each got total doses of 0.83, 1.66, 2.50, 4.16, and 8.33 mc hr., respectively.

It can be seen from this report that the length of each application of radium D, the number of applications, and the interval between doses have little effect upon the final outcome of therapy as long as the total therapy is sufficient.

The follow-up period in these cases varied from 1½ months to 12 months, with an average of 6.5 months. A long post-therapy observation time is probably not necessary in these cases, as the maximum effect of treatment may be ascertained within two or three months after its cessation. Little improvement occurs after this period.

The results of treatment in this group are encouraging. Eighteen eyes (42.8%) were cured; 16 (38.1%) showed improvement, and with only 8 (19.0%) did treatment fail. One patient did not complete her therapy.

On breaking down the statistics into cases of primary pterygium, recurrent pterygium, and pseudopterygium, it was found that, of the primary cases, 10 (38.4%) represented cures; 11 (42.3%) improvement, and 5 (19.2%), therapeutic failures. Of the nine recurrent pterygia treated, four (44.4%) were cured, four (44.4%) showed improvement, and one (11.2%) represented failure of therapy. Six pseudopterygia were treated with radium, with cure in five cases (83.3%) and failure in one (16.7%). The standards established in this study for these three categories of final results should be clarified:

1. The eye is said to be cured when there is absence of corneal vascularization and of growth in the follow-up period.

2. The eye shows improvement when there are marked decrease in vascularity to the corneal part of the pterygium and absence of growth in the follow-up period.

3. Treatment has failed when the eye shows little or no decrease in vascularity and/or increase in growth during the follow-up period.

In only 2 of the 43 eyes was there complete absence of any evidence of previous existence of pterygium on the eye in question. All the remaining eyes showed the pterygium still in place on the cornea, appearing as a gray-white fibrous ghost of the former growth. This condition was present whether the condition was considered improved or cured, and was certainly present if treatment had failed. Determination of the amount of residual vascularity of the growth is used to place it in one of the three categories noted above, but all types show the fibrous "base" of the growth attached to the cornea. This condition seems to me to represent an "esthetic failure" of treatment, even though it may be called a "medical cure." Most patients come to have the growth removed because it is unsightly, not because of its potential ability to decrease visual acuity. Therefore any therapeutic result short of entire obliteration of the corneal section or scar, at least, of the pterygium is to him a failure, especially if he can see that the remaining tissue occupies the same position that the growth did previously.

In addition, it must be remembered that only the vascularity of the corneal part of the pterygium was considered. This was the part of the pterygium receiving most intense radiation. Although a considerable amount of the total therapy was applied to the body of the pterygium, and although in most cases the response of the body closely followed that of the head and neck, this was not always true. Many patients returned with growth arrested, with corneal vascularity gone, but with considerable redness remaining in the pterygium body. This remaining vascularity was not taken into account when the results of the case study were classified because I was interested primarily in a medical cure—arrest of growth.

In two points, then, pterygium transplantation has an advantage over beta-ray therapy: (1) It removes the growth from the cornea, and (2) the vascularity of the body disappears after operation.

COMPARISON OF VARIOUS TYPES OF THERAPY

It is difficult to compare the various kinds of therapy for pterygium, simply because the answer is one of quality, and not of quantity.

Of the 85 eyes studied, surgical treatment resulted in failure in 15% and beta radium therapy in 19%, percentages which are about the same. However, patients

in the first group underwent a surgical procedure, with all its mental hazards, whereas those in the second group were spared this but had to return for prolonged treatments. If surgery was successful, complete removal of the growth was obtained. This is not true of radium D therapy, where parts of the pterygium, although avascular, may remain in situ.

In addition, control and double therapy must be considered. The physician is almost directly responsible for the postoperative condition of the eye, as during the operative procedure he may resect or alter the tissues as he wishes. With radium D therapy, however, he can treat only the various pterygium areas and hope that these areas will atrophy. He has no direct control of the tissues to be ablated. Surgery has an additional advantage in that it may be performed first, and then if it fails, radium D therapy may be instituted. Surgery would be rendered more difficult if the procedures were reversed.

Hilgartner and associates reported 10 cases of pterygium which was treated surgically, followed by x-ray therapy, begun on the fifth postoperative day. No recurrences were noted. This type of therapy, although effective in a small series of cases, needs to be proved effective in larger groups of cases. In addition, the hazards of x-irradiation of the ocular tissues should not be underestimated, even if carried out in a controlled manner. If ocular tissues, on the other hand, are to be exposed to gamma rays, it would be much better to use a radium element or radon applicator, with which therapy time is shorter, extraocular appliances are not needed, and the physician has the convenience of using a smaller instrument. Therefore, despite cures with postoperative x-ray treatments reported in a few cases, I believe that use of some type of radium or radon applicator is better therapy.

SUMMARY AND CONCLUSIONS

The 10-mc. radium D applicator of Swanberg is effective in the therapy of all types of pterygium.

1. Such therapy obliterates the vessels and stops the growth of primary flat pterygia, but usually leaves a scar (pterygium ghost) from the cornea to the conjunctiva, representing the former pterygium.

2. The same is true of the primary meaty and vascular pterygia, but a scar always remains, possibly with some vascularity of the pterygium head.

3. Recurrent flat or meaty pterygia react to therapy as do primary growths.

4. Radium D therapy of pterygia often leaves considerable vascularity remaining in the pterygium body despite cessation of growth and absence of vascularity in the pterygium head.

5. Pseudopterygium responds well to radium D therapy. The results, however, depend upon their cause and pathologic anatomy.

When scheduling radium D therapy for pterygia, more attention should be paid to the final total dose than to the manner in which individual doses are applied; that is, the time per individual dose and the interval between them are of less importance. Any convenient routine may be followed, one week being the minimum safe interval between doses. The total dose should be more for the meaty, vascular pterygia than for the flatter, more membranous type. The approximate total dose should be 5 mc.-hr. for the former and 2.5 mc.-hr. for the latter.

Virtually no temporary or permanent harmful side-effects were obtained from irradiation in this series of cases.

Judging from cell susceptibility, beta-irradiation should be more effective if used early (during the first week) on a postoperative pterygium area to stop recurrence than if used on a primary or fully recurred pterygium. Such therapy was not studied in this series.

In conclusion, then, I believe that the McReynold transplantation plus early postoperative use of the radium D applicator is the best therapy for pterygia now available.

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EVALUATION OF FIVE NEW CYCLOPLEGIC DRUGS

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IN A SEARCH for an ideal cycloplegic agent, five new anticholinergic drugs have been evaluated at the Research and Refraction Departments of the Wills Hospital.

1. Methantheline bromide (banthine®; β-diethylaminoethylxanthene-9-carboxylate methobromide) [1]

2. D-2 (2,2-diphenyl-4-dimethylaminoethyl-1,3-dioxolane methobromide) [2]

3. Three drugs all of which are esters of disubstituted acetic acids and are known for the time being as Compound 75 G. T., Compound 92 G. T., and Compound 93 G. T.[3]

PRESENT INVESTIGATION

Drug Testing.—1. Solutions were instilled into the conjunctival sac of the unanesthetized eye of white albino and chinchilla rabbits. The effect on the pupillary size and light reflex was observed. The duration of mydriasis was noted. If satisfactory mydriasis was produced with no local irritation, human studies were considered.

2. Weak dilutions were instilled in human eyes, preferably eyes with blue irides.

3. If cycloplegia was noted, then solutions of various strengths were used in the eyes of dark-skinned Negroes. The patients were given refraction after one hour, and the amount of residual accommodation was determined by the method previously described by Prangen.[4] All the patients used in the studies were those whose visual acuity was or could be improved to 6/6. All were under the age of 40 and were subjectively reliable.

4. Time for recovery of accommodation was determined.

Method of Administration.—One drop of the solution tested was used in each eye. The instillation was repeated in five minutes, and examination was performed 60 to 90 minutes after the first instillation.

From the Research and Refraction Departments of the Wills Hospital.

Presented at the Fourth Annual Wills Hospital Conference, March, 1952.

Chief, Refraction Department, Wills Hospital (Dr. Gettes); Director, Research Department, Wills Hospital (Dr. Leopold).

1. G. D. Searle & Company.

2. Wm. S. Merrell Company.

3. Schieffelin & Company. The compound referred to as 75 G.T. is marketed under the trade name "cyclogel."

4. Prangen, A. DeH.: Some Problems and Procedures in Refraction, Arch. Ophth. **18:** 432, 1937.

1. *Methantheline.*—A 0.5% solution of methantheline bromide in isotonic sodium chloride solution was instilled into 32 eyes (16 patients). These patients were all fair-skinned with light irides.

A 1% methantheline solution in 1 : 50,000 benzalkonium chloride (as a wetting agent) was used in 10 patients.

A 2% methantheline bromide solution in 1 : 50,000 benzalkonium chloride was likewise used in 10 patients.

Results:

A. Of the patients tested with 0.5% methantheline bromides, only five (30%) had a residual accommodation of 2.5 D. or less. Three patients had neither mydriasis nor cycloplegia. All of these patients were examined with a solution of 2.5% dibutoline sulfate (dibutylcarbonate of dimethylethyl-2-hydroxyethyl ammonium sulfate) with 2% homatropine hydrobromide, and all were found to have less than 2.25 D. of residual accommodation.

B. Only 3 of the 10 patients tested with 1% methantheline bromide had a residual accommodation of 2.5 D. or less. These patients, when reexamined with the homatropine and dibutoline mixture, all had less than 1.5 D. of residual accommodation.

C. Only two of the patients tested with 2% methantheline bromide had less than 2.5 D. of accommodation, although all had more than 4 mm. of mydriasis. With the homatropine and dibutoline solution, all 10 patients had less than 2.0 D. of accommodation. With the 2% dilution, all the patients complained bitterly of burning and tearing. In five of the patients the symptoms persisted at least 30 minutes.

It appears from these results that (*a*) a 1% solution of methantheline bromide in benzalkonium chloride is an adequate mydriatic when used topically, (*b*) the cycloplegic effects are not as pronounced as the commonly used shorter-acting cycloplegics, and (*c*) solutions stronger than 1% are irritating, and therefore not practical.

2. *D-2 (2,2-diphenyl-4-dimethylaminoethyl-1,3-dioxolane) methobromide.*—A 3% solution of D-2 methobromide was instilled into the eyes of 25 patients (15 Negroes and 10 white persons).

Results: Of the 50 eyes tested with 3% D-2 methobromide, only 7 had a residual accommodation of 2.0 D. or less. In only 15 eyes was the residual accommodation less than 2.5 D. In this group with less than 2.5 D. of residual accommodation, only four eyes were of Negro patients. Twenty-two eyes had neither mydriasis nor cycloplegia. All the patients complained bitterly of the burning and smarting of the eyes.

These results suggest that 3% solution of D-2 methobromide is an unsatisfactory drug for refractive purposes, since (*a*) 75% of the subjects tested had a residual accommodation of more than 2.5 D., (*b*) 31% of the patients failed to show mydriasis, and (*c*) all patients complained of subjective burning after instillation.

3. *Compounds 75 G. T., 92 G. T., and 93 G. T.*—Treves and Testa [5] synthesized a series of alkyl aminoalkyl and N-piperidinoalkyl esters of (1-hydroxycycloalkyl)

5. Treves, G. R., and Testa, F. C.: Basic Esters and Quaternary Derivatives of β-Hydroxy Acids as Antispasmodics, J. Am. Chem. Soc. **74**:46, 1952; personal communication to the authors.

arylacetic acid. Ehrenberg, Ramp, Blanchard, and Treves [6] reported on 38 of these new synthetic drugs, of which 3 showed mydriatic effects similar to those of atropine. The 38 compounds are the hydrochlorides and the methohalides of β-hydroxyacids of the general structural formula:

$$\begin{array}{l} R\text{—}CH\text{—}R^{1} \\ \quad\quad | \\ \quad COO\ (CH_2)_2\text{—}R^{11} \end{array}$$

where R is a 1-hydroxycycloalkyl group, R^{1} is a phenyl or a 4-methoxyphenyl group, and R^{11} is a substituted amino group or a 1-piperidyl group.

All these compounds are esters of disubstituted acetic acids. These authors, in testing these solutions for mydriatic activity in rabbits, found that the quaternary methohalides caused incomplete mydriasis, whereas the tertiary compounds proved to be satisfactory mydriatics. These three ternary compounds were subjected to clinical evaluation, one of which, Compound 75 G. T., has been preliminarily reported by Priestley and Medine.[7]

TABLE 1.—*Cycloplegic Activity of 75 G. T., 92 G. T., and 93 G. T.*

Amount of Residual Accommodation, D.	No. of Eyes		
	0.5% 75 G. T.	0.5% 92 G. T.	0.5% 93 G. T.
0-1.5	50	36	57
1.5-2.0	16	26	30
2.0-2.5	0	13	2
More than 2.5	10	15	11
No cycloplegia; no mydriasis	24	10	0

Priestley and Medine measured the mydriatic effect of the 0.5% solution of Compound 75 G. T. in 100 subjects and the cycloplegic effect in 50 patients, presumably all of the Caucasian race. They reported an average residual accommodation of 1.25 D., whereas the average for the same patients with 5% homatropine hydrobromide was 2.0 D. In their series, maximal cycloplegia approximated maximal mydriasis, and recovery from cycloplegia was complete in less than 20 hours.

Each of these three compounds (75 G. T., 92 G. T., and 93 G. T.) was tried on 100 eyes. All these eyes were in dark-skinned Negroes. The only eyes used were those in which visual acuity could be improved to 6/6, and the only patients used were those who were subjectively reliable. All these patients were from the refraction clinic of the Wills Hospital; all were between the ages of 20 and 40 years; all were studied by the same examiner. The solutions were in a concentration of 0.5% in a boric-acid borate buffer of approximately pH 5.7 with 1:50,000 benzalkonium chloride added as a preservative. One drop was instilled in each eye and the instillation repeated in five minutes. Examination was done one hour after the last instillation.

The results are shown in Table 1.

6. Ehrenberg, M. H.; Ramp, J. A.; Blanchard, E. W., and Treves, G. R.: Antispasmotic Activity of Basic Esters and Quaternary Derivatives of β-Hydroxy Acids, personal communication to the authors.

7. Priestley, B. S., and Medine, M. M.: A New Mydriatic and Cycloplegic Drug, Am. J. Ophth. **34**:572, 1951.

Considering all cyclopegics that consistently produce a residual accommodation of 2.5 D. or less as being 100% effective (Prangen), the efficiency of these agents and that of standard drugs may be compared (Table 2).

In all cases, with Compounds 75 G. T., 92 G. T., and 93 G. T., cycloplegia disappeared within 24 hours. Over 50% of the patients receiving instillations of Compound 93 G. T. had mydriasis, but no cycloplegia, after 24 hours.

Pilocarpine nitrate, 2%, was instilled in 10 patients in each group at the completion of the examination. This appeared to hasten the recovery from cycloplegia, as all patients could read after six hours with any of these drugs. None complained of any local discomfort, and in no case was any toxic systemic manifestations noted.

Intraocular pressure was measured in all patients, and no apparent increase was noted.

TABLE 2.—*Effectivity of Cycloplegics on Eyes of Patients with Dark Irides and with Darkly Pigmented Skin*

Drug Used	% Effective*
4% homatropine hydrobromide in 1% hydroxyamphetamine (paredrine®) hydrobromide	54†
0.5% Compound 75 G. T.	66
0.5% Compound 92 G. T.	75
2% homatropine with 2.5% dibutoline sulfate	76†
0.5% Compound 93 G. T.	89
1% atropine sulfate	100†‡

* Percentages are based on a residual accommodation of 2.5 D. or less.
† Gettes, B. C.: Arch. Ophth. **43**:446, 1950.
‡ Prangen.[4]

SUMMARY

Five parasympathomimetic blocking agents were tested clinically in dark-skinned Negro patients and their cycloplegic effects evaluated. The results were as follows:

1. Methantheline (banthine®) bromide in 0.5 and 1.0% solutions is an inadequate cycloplegic for routine examination.

2. D-2 methobromide in a 3% solution is an inadequate cycloplegic.

3. Compounds 75 G. T., 92 G. T., and 93 G. T. in 0.5% solution are more effective than 4% homatropine hydrobromide solution in 1% hydroxyamphetamine (paredrine®) hydrobromide solution, which is now the most commonly used shorter-acting cycloplegic combination.

(*a*) Of these, Compound 93 G. T. appears to have the most profound effect.

(*b*) The time of recovery from cycloplegia for all these preparations was less than 24 hours.

(*c*) None of these solutions produced any local or systemic toxic effect.

NORMAL AND REVERSED VISION IN TRANSPLANTED EYES

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A SYSTEMATIC study of the morphology and function of the visual mechanism in the vertebrates reveals a variation in visual capacity and a wide alteration in the optic centers of the brain due to the development and elaboration of addition structures. On the other hand, the general morphological pattern of the eye as a whole or of its parts is quite similar in all these animals. This is particularly true when we consider certain features of that essential delicate membrane the retina, upon which many of the following experiments are focused.

In all vertebrate eyes a prominent pigment epithelium marks the basal layer of the retina, above which lie the three characteristic nuclear layers, namely, the rod-cone elements, the intermediate bipolar cells, and the ganglion cells. Lacking a better term, I shall identify these layers, along with their intervening reticular zones and the inner and outer membranes, as the neural retina. It will be shown in the following experiments on certain vertebrate eyes that this unit can be completely regenerated from another retinal unit, namely, the basal-lying retinal pigment epithelium.

This neural retina, except in larval forms of amphibians, degenerates in all eyes, from fishes to man, when the retina is temporarily deprived of its blood supply. Up to now my studies of all classes of vertebrates have shown that the lost neural retina is replaced only in the case of amphibians, in which it is regenerated from the surviving retinal pigment epithelium (Stone [1]). This is best demonstrated in experiments on the adult salamander eye. The retinal pigment epithelium can be slowly denuded within three weeks through the degeneration of the overlying neural retina in a transplanted eye, or it can be exposed immediately by directing from a micropipette a gentle stream of dilute saline solution through a large opening in front of the eye. This dislodges (Fig. 1) the neural retina from the retinal pigment

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This study was aided by grants from the James Hudson Brown Memorial Fund of the Yale University School of Medicine, and the United States Public Health Service.

1. Stone, L. S.: (*a*) Doyne Memorial Lecture: Return of Vision and Funtional Polarization in the Retinae of Transplanted Eyes, Tr. Ophth. Soc. U. Kingdom **67**:349-367, 1947; (*b*) Neural Retina Degeneration Followed by Regeneration from Surviving Retinal Pigment Cells in Grafted Adult Salamander Eyes, Anat. Rec. **106**:89-110, 1950; (*c*) Role of Retinal Pigment Cells in Regenerating Neural Retinae of Adult Salamander Eyes, J. Exper. Zoöl. **113**:9-32, 1950.

cells, so that it can be floated out of the eye intact. The histological appearance of an excised neural retina in a typical case is shown in Figure 3 *A*. In the same eye 57 days later (Fig. 3 *G*) regeneration had been completed.

The denuded retinal pigment epithelium cells (Fig. 3 *B*) soon change their form and function, transform from flattened to columnar cells, and undergo mitosis (Fig. 3 *C*). The daughter cells which face inward towards the vitreous chamber lose their pigment and form a sharply defined layer (Fig. 3 *D*), which by repeated cell divisions (Fig. 3 *E*) and differentiation (Fig. 3 *E* and *G*) gives rise to the new neural retina. The daughter cells which retain their pigment remain at the base as a single layer, reestablishing the retinal pigment epithelium. While differentiation of the regen-

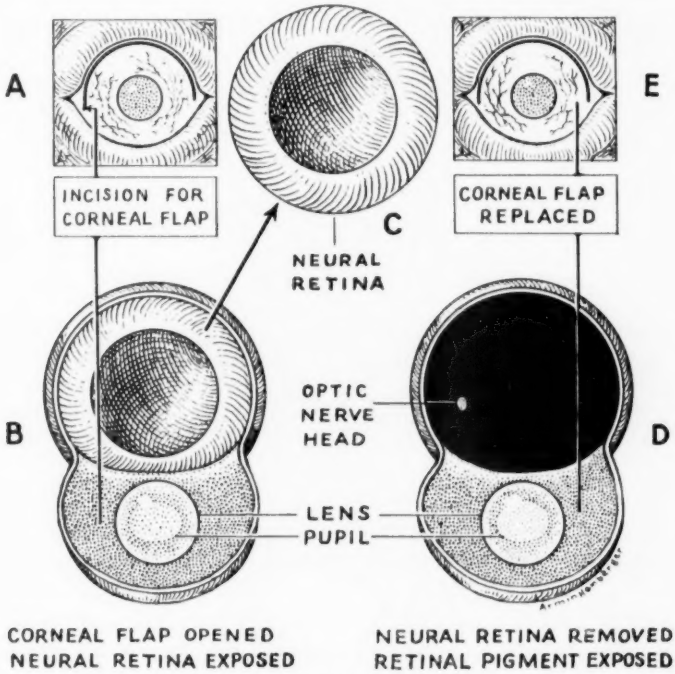

Fig. 1.—Steps (*A*, *B*, *C*, *D*, and *E*) in opening and closing a corneal flap in a salamander eye to expose and remove the neural retina intact, leaving the retinal pigment cells in place. The neural retina (*C*) is floated out by means of a stream of Ringer's solution from a micropipette.

erated neural retina is being completed, a new optic nerve grows out from the ganglion cells of the retina, following the old pathway of the degenerated one. These new fibers cross the chiasm and enter the proper brain centers in the optic tectum to establish return of vision.

The activity of these retinal pigment cells can also be closely followed in more restricted wound areas in the retina. If an incision is made in the cornea sufficiently large to remove the lens and through this slit an especially prepared pipette is then inserted, a limited segment of neural retina can be gently sucked out, leaving a well-defined denuded area of retinal pigment epithelium. The latter responds by

the gradual changes that lead to the development of new neural retina tissue, which fills the space without any contribution from the surrounding intact neural retina cells. In very small localized wounds where a few neural retina cells are removed or caused to degenerate the underlying retinal pigment cells respond by marked proliferation and mass migration into the wound to fill the gap. There is a tendency for them to become depigmented later and differentiate into neural retina elements. These proliferating pigment cells may even wander in among the cells of the adjacent intact neural retina. In this respect they appear to be similar to the depigmented retinal pigment epithelium described by Cogan [2] as invading the human retina.

Among my various experiments concerned with the relation of retinal pigment cells to different types of wounds it was found that where surviving neural retina folds became slightly detached the underlying retinal pigment cells produced a thick black localized membrane, which persisted. If the surviving retinal fold was considerably elevated, the detached retinal pigment cells then formed a secondary neural retina. Lack of contact with, and sufficient isolation from, the neural retina elements

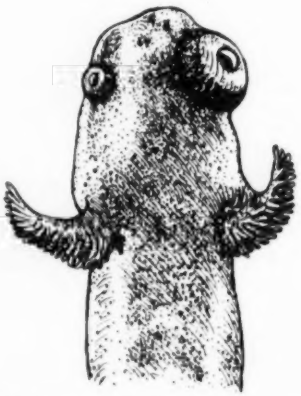

Fig. 2.—Small salamander larval host (Amblystoma punctatum) with the transplanted right eye of the large tiger salamander (Amblystoma tigrinum). × 6.

apparently releases the regenerative capacity of these pigment cells. In fact, the retinal pigment epithelium can still give rise to neural retina in the salamander eye if it is detached and implanted into the aqueous chamber or in the pupillary space of another eye. Whether or not the same hidden qualities exist and can be unmasked in the retinal pigment cells of other vertebrate eyes is being further investigated.

Since the neural retina is so readily replaced in the amphibian eye, I have found it a unique tool in devising new experiments for studying the organization and development of the visual mechanism. These opportunities are not offered by the eyes of other groups of vertebrates. This is indicated by the fact that I have shown return of vision four times in the same eye repeatedly transplanted (Stone and Farthing [3]). The grafts will remain functional and in normal condition for several

2. Cogan, D. G.: Symposium: Primary Chorioretinal Aberrations with Night Blindness: Pathology, Tr. Am. Acad. Ophth. **55**:629-661, 1950.

3. Stone, L. S., and Farthing, T. E.: Return of Vision 4 Times in the Same Adult Salamander Eye (Triturus viridescens) Repeatedly Transplanted, J. Exper. Zoöl. **91**:265-285, 1942.

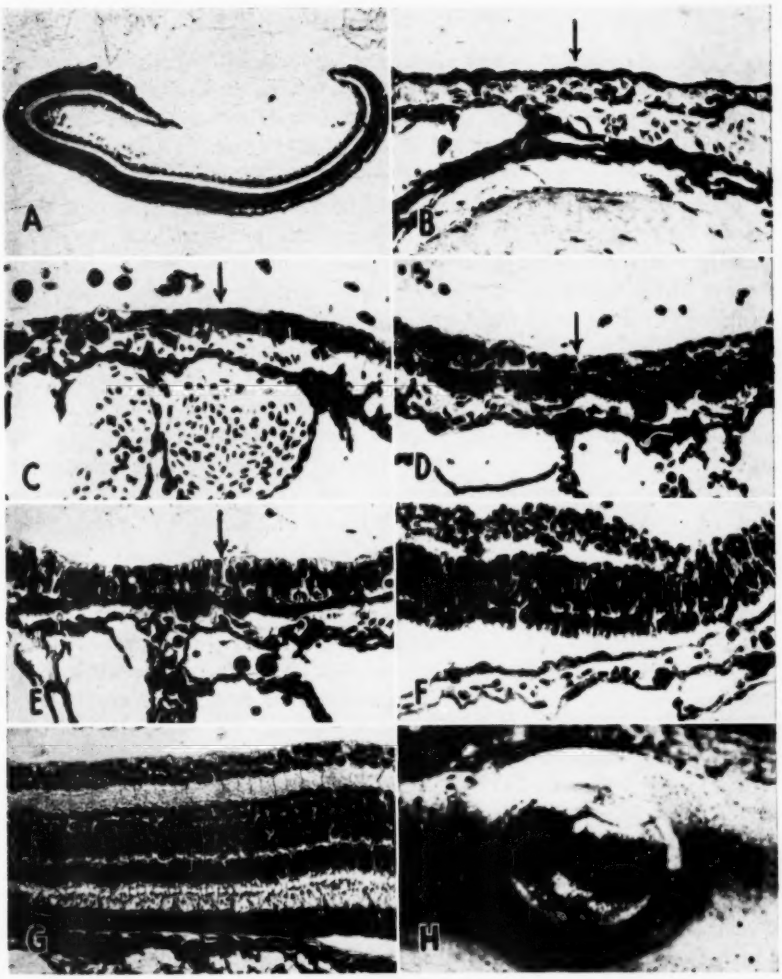

Fig. 3.—*A*, microscopic appearance of neural retina which was removed intact from the eye shown in *G*, where it had later completely regenerated. *A* to *H* concern adult eyes of the vermilion. spotted newt (Triturus viridescens). *A* to *F* show progressive stages of retinal regeneration. × 40.

B, flattened denuded retinal pigment epithelium, indicated by arrow, six days after removal of entire neural retina. × 130.

C, enlarged retinal pigment cells preparing for mitosis, 10 days after operation. × 130.

D, layer of depigmented cells from which the new neural retina is developing. 12 days after removal of original neural retina. These cells developed from the retinal pigment cells beneath. × 130.

E, rapid mitosis taking place in the regenerating neural retina, 20 days after operation. × 130.

F, differentiation of retinal layers, beginning in a limited area of the regenerating neural retina, 30 days after operation. × 130.

G, completely regenerated functional retina 57 days after the entire neural retina (*A*) had been removed. × 130.

H, transplanted, 180 degree rotated eye with reversed vision for four years seven months. Normal vision was immediately restored by cutting the conjunctiva and ocular muscles and twisting the eye in situ back to normal position, without injury to the retina, optic nerve, or blood vessels. × 8.

years (Fig. 3 *H*; Stone [1a]). The eye can be refrigerated for a week and then successfully transplanted (Stone [4]). The eyes of a number of species of salamander can be transplanted to a host of an entirely different species, where they become functional organs of vision (Stone,[5] Stone and Ellison,[6] Stone [7]). This demonstrates that both the eyes and the optic tectum of the brain in the various species are similarly organized, since they can function in vision when brought into these combinations. These experiments provide new methods by which one can study the contributions which both the eye and the brain make to visual function. For example, if the eye of one species of salamander which normally has a low visual acuity is transplanted to the host of another species with high visual acuity, the host then has sharper vision with the grafted eye than the donor normally exhibits. Therefore the brain of the new host must have been a contributing factor in raising the visual acuity in this combination. On the other hand, the visual acuity with the new eye is not as high as this host possesses when its brain is connected with its own homoplastically grafted eye. The eye of the donor may therefore be responsible for lowering the visual acuity in this combination. This method of study is being explored further with other species in which eyes and tissue of reciprocal hosts are mutually tolerated.

How successfully the normal morphological picture can be restored in the regenerated retina is shown by comparing Figure 3 *B* and *F*. A study of the pattern of vision in various types of transplanted eyes also reveals that the retinal fields are reestablished as they were originally and that they function according to their orientation (Stone,[8] Sperry [9]). Vision is normal if the grafted eye is normally oriented. It is reversed in all the functional quadrants of the regenerated retina if the eye has been excised, rotated 180 degrees, and reimplanted in the orbit. The reversed vision is the same as in a control experiment, in which a normal eye is merely rotated 180 degrees in situ and fixed in place after cutting only the conjunctiva and muscular attachments. This method preserves the blood supply, optic nerve, and original retina, so that visual function is uninterrupted. Furthermore, if the right and the left eye are exchanged and properly oriented, either the dorsal and ventral or the nasal and temporal quadrant can be reversed, leaving the remaining two quadrants normally oriented in the same eye. This results in unique visual behavior, for as soon as the retina is regenerated and connected with the brain by

4. Stone, L. S.: Return of Vision in Transplanted Adult Salamander Eyes After 7 Days of Refrigeration, Arch. Ophth. **35**:135-144, 1946.

5. Stone, L. S.: Heteroplastic Transplantation of Eyes Between the Larvae of 2 Species of Amblystoma, J. Exper. Zoöl. **55**:193-261, 1930.

6. Stone, L. S., and Ellison, F. S.: Return of Vision in Eyes Exchanged Between Adult Salamanders of Different Species, J. Exper. Zoöl. **100**:217-227, 1945.

7. Stone, L. S.: Development of Normal and Reversed Vision in Transplanted Eyes, Proc. 16th Internat. Congress Ophth., London **2**:644-648, 1950.

8. Stone, footnotes 4, 1, and 7.

9. Sperry, R. W.: Optic Nerve Regeneration with Return of Vision in Anurans, J. Neurophysiol. **7**:57-70, 1944; Restoration of Vision After Crossing of Optic Nerves and After Contralateral Transplantation of Eye, ibid. **8**:15-28, 1945.

the new optic nerve, vision is reversed in the reversed quadrants and normal in the other two fields of the same eye. Motion picture records have been made of the results of these experiments.

The first signs of return of vision are best detected when the host possesses only one eye, the transplanted one. Vision usually returns in the grafted adult salamander eye between two and three months after operation. This is at a time when the regenerating retina is completing its differentiation. While the new retina is gradually taking on a normal appearance, the first signs of the returning visuomotor reactions are weakly expressed as the animal responds to the moving lure or to the alternating black and white stripes on a rotating drum. In two or three weeks these reactions become stronger, and in homoplastic transplants the visual acuity later usually becomes as sharp as it was originally, before operation. Animals with normally oriented eyes swim freely in all directions and snap at or follow a lure, such as a dark object impaled on the end of a slender wire, approaching any of the four quadrants in the field of vision. By head and body movements the animal follows vertical black and white stripes on a drum if the stripes are rotating temporonasally through the field of vision of either eye. These compensatory movements are not called forth if the stripes move nasotemporally through the field of vision of either eye. Therefore with this method there is a perfect test for a left eye (clockwise rotation) and a right eye (counterclockwise rotation).

An animal with a functioning eye rotated 180 degrees shows marked abnormal swimming movements toward the blind side as soon as the normal, intact eye, on the other side, has been removed. All the visuomotor responses to a moving lure are reversed, and the head and body movements to the stripes on a drum moving in a direction from the reversed temporal to the reversed nasal field of vision are in a direction opposite (the reverse of) that of the rotating drum.

These abnormal swimming reactions and reversed visual responses persisted in adult animals with rotated eyes kept over 4½ years. The grafted eye of one of these salamanders is shown in Figure 3*H*. At that time all normal visuomotor reactions were immediately restored by merely cutting the conjunctiva and ocular muscles and rotating the eye back to normal orientation without disturbing the vascular supply to the retina or injuring the optic nerve while twisting it.

The functional organization of the retina in the salamander eye is determined at an early optic-cup stage in development, before the future retina has even differentiated. This was proved by excising embryonic eyes at all stages of development, rotating them 180 degrees, and reimplanting them. Later visual tests showed that hosts with eyes which had been rotated at a certain time in the early optic-cup stage or later had acquired reversed vision. All animals in which the eyes were rotated before that time developed normal vision.

At the time when the future polarization of the retina is determined the optic cup can be excised and transplanted to the body wall of another host, where it will complete its development independently of any contact with the brain. At the end of six to eight weeks the transplanted eye has the same appearance as the normal eyes of the host. If it is then dissected from the body wall, its short optic nerve cut to stimulate regeneration, and the eye then transplanted to the denuded orbit of another animal of similar age, it can soon become a functioning eye. Since the retina of a transplanted larval eye does not degenerate (Stone [5]), the optic nerve starts

regeneration immediately and soon connects with the brain for the first time. This is accomplished within a month. Vision is normal if the graft is normally oriented and is reversed if it is rotated 180 degrees. However, the marked abnormal swimming behavior so prominent with rotated adult eyes is not developed. This is a visuomotor reaction which apparently develops either in late larval life or after the metamorphosis of the host. This interesting behavior response is being studied in greater detail in other experiments, focused on the development and elaboration of visual patterns as animals approach maturity.

In all stages of development the embryonic eyes can be exchanged between two different species of salamander, one of which (Amblystoma tigrinum) grows to be several times as large as the other (Amblystoma punctatum). The grafted eyes develop at their own species rate. Therefore the contrast between the large eye on the small animal (Fig. 2), and vice versa, is very striking. Each host develops good vision with the other species' eye. Some of the small hosts appeared to show more acute vision with the large-eye graft than with their own (control) eyes. How much this was due to the hyperplasia of the optic tectum in the host produced by the ingrowing optic fibers of the large grafted eye is not yet certain. The large hosts with the small transplanted eye showed no measurable differences in the vision of the normal and that of the grafted eye. Hypoplasia of the optic tectum in the brain of the host was produced by the small-eye graft in these experiments.

Rotation of the embryonic eyes of these two species showed that the retinal quadrants are polarized at the early optic-cup stage in each of them. When the eyes were exchanged this time, good normal vision resulted later if the grafts were normally oriented. If the grafts were rotated at 180 degrees, reversed vision was later demonstrated, but not the abnormal swimming reactions. These types of grafts provide a new approach to the study of the development of vision which will be very fruitful in obtaining a better understanding of the factors influencing the organization of the central-nervous-system portion of the visual mechanism. Knowledge gained in this field has a broad application to the study of vision in other vertebrates, including the human subject.

ABSTRACT OF DISCUSSION

Hermann M. Burian, Iowa City: Ever since I became acquainted with Dr. Stone's studies I have been fascinated by them. To one who has been trained in human physiology of vision his results appear almost fantastic; yet to such a one they are of paramount importance.

The fact that inversion of the retinal field in Amblystoma and Triturus by one means or another causes a permanent inversion of the visual field of these animals is experimental evidence for the nativistic concept of the physiologic basis of visual orientation. It proves that the physiologic basis of visual orientation is not acquired by any learning process but is due to anatomic and physiologic relationships which come about through normal processes of development, and it further proves that these relationships are immutable.

What applies to Amblystoma and Triturus applies also to man. Man's visual orientation is fundamentally innate, i. e., determined by the phylogenetically acquired anatomic and physiologic organization of his visual system. But there is this difference between man and the salamander: Man does have the ability under specified conditions of adapting himself to inversions or distortions of his visual field. If man's visual field is inverted, as in the experiments of Sutton, or if discrepancies between the two eyes are introduced by means of size lenses, dis-

arrangements and stereoscopic distortions of space occur to which an adjustment takes place after a certain length of time. Man learns how to reorient himself in space. But this is not due to changes in the fundamental anatomic and physiologic relationships in the visual system. Rather, it is due to the fact that man can make use of secondary factors in spatial orientation, such as the uniocular clues to depth localization. This, apparently, Amblystoma cannot do. Experimental evidence that the fundamental relationships remain as unchanged in man as in Amblystoma is to be found in my studies on the effect on spatial orientation of meridional size lenses. If the lenses were worn for some time, the initial spatial distortions disappeared, but only so long as the observer remained in surroundings abounding in perspective clues. In surroundings in which stereoscopic clues predominated, the spatial distortions reappeared immediately, regardless of how long the size lenses had been worn—proof that there had occurred no change in the fundamental physiological relationships of the visual system.

Thus, Dr. Stone's work, which may appear to be far removed from our sphere of interest, actually ties in very closely with problems in binocular vision and ocular motility which are of fundamental, as well as clinical, importance.

We are all very much indebted to Dr. Stone for coming to talk to us about his admirable investigations.

IDIOPATHIC DETACHMENT OF THE RETINA

Analysis of Results

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THE 618 cases of "idiopathic detachment of the retina" reviewed are those of patients examined and treated at the retina service of the Massachusetts Eye and Ear Infirmary between 1947 and July, 1951. During this period, operation has been performed in some cases without the participation of the retina service, and these cases have not been included in the group. Additional cases omitted from the group are those in which operation was refused, the cases of subclinical detachments, and a small number of cases in which insufficient data were available.

The group represents the private patients of many different attending physicians and patients from the Infirmary clinics. The operators have been the senior and junior attending physicians and the retina service physicians, as well as the resident staff. Examinations before, during, and after operation have been carried out by these men and the retina service. During the last two years of the period presented a number of less experienced physicians have participated in the program of the retina service. Thus, the examinations and operative assistance of the retina service are represented during the last one-half as reported by more than one observer. The data presented were collected by us from the records of the retina service, the hospital records, and the private records of the attending physicians.

What is a successful case? In this paper it is considered to be one in which reattachment of the retina persists for six or more months after retinopexy. The reattached retina may show slowly regressing and fairly flat fixed folds in the attached area, central to the treated sites, or residual detachment peripheral to the area of treatment. Good vision, although sought in all cases, cannot be a measure of success. Central vision often may be poor, and, indeed, the patient may consider his case one of a failure. It is obvious that the criterion of persisting reattachment must be used in determining a successful case. To obtain a six-month follow-up period, it has been attempted often to pursue the final result through the attending or referring surgeon. Most of the patients, however, were followed for six months or more by members of the retina service.

Despite this, there remain 65 cases of reattachments in which evidence of continued success six months after operation has not been obtained. These will be mentioned as such, separately.

This work was done at the Retina Service of the Massachusetts Eye and Ear Infirmary.
Read before the Section on Ophthalmology at the One-Hundred and First Annual Session of the American Medical Association, Chicago, June 12, 1952.

Failures are recorded in cases in which reattachment had not occurred when the patients were last seen, at discharge from the hospital or during their outpatient examinations during the following six months.

Examination was made in 618 cases of "clinical idiopathic detachments of the retina." The patients sought, or were referred for, possible surgical care. Operation was performed in 525 cases; in the remaining cases the condition was deemed inoperable and the patients were advised that no operation should be performed. Thus, we must conclude that treatment was a failure in 15% of all the cases, even before surgery was attempted.

An operation for detachment of the retina was performed on 525 eyes. Three hundred sixteen eyes were successfully operated on according to the conditions previously presented. In 65 eyes the operation appears to have been successful, but a six-month follow-up period has not been completed. In 144 cases the retina

TABLE 1.—*Data on Cases of Clinical Idiopathic Detachment*

Total no. cases reviewed	618
Cases in which operation was advised against	93
Operation cases	525
No. of reattachments	381
No. of reattachments with six months' follow-up	316
No. of reattachments without six months' follow-up	65
No. of failures	144
Cases in which reoperation was refused	9
No. of complete failures	135
Total no. of cases used for this study	451

TABLE 2.—*Successful Operations*

	No. of Cases	Per Cent
Six months' follow-up *	316/451	70
Total no.	381/516	74

* All subsequent analyses are derived from this group of patients.

failed to become reattached after operation. However, in nine of these cases reoperation was refused, and they should be excluded from the group of failures. The failures would then be 135.

Thus, the retinas in 70% (316) of the eyes operated on were successfully reattached. If the 65 additional eyes can be later included, the success would be 74%. However, consideration of the original 93 eyes not operated on presents a total of 228 failures among all the cases of clinical idiopathic detachment. The percentage of cases in which operation was successful would then be 57%. Were reattachment in the 65 additional cases demonstrated to be really successful for six months, the percentage of successful cases would be 62% of all the cases seen.

Why were 93 of the 618 patients advised against operation? It is obvious that success and failure of treatment of the retinal detachments may vary with the selection of the patients for the operation. Of the 93 patients "advised against" operation, the outlook seemed hopeless for all but 2. These two, however, were not physically able to tolerate treatment. The other patients had detachments of long duration, with more than one of the following findings: total separation, atrophic

retina, extensive fixed folds, massive retraction of the vitreous, and retinitis proliferans. Most of the eyes either were blind or had vision approximating light perception only. However, 14 patients counted fingers at 1 ft. (30 cm.), 7 had vision of approximately 20/300.

The examinations of the patients by the retina service before, during, and after operations were performed in the manner previously described by Dr. C. L. Schepens. This includes determination of visual acuity; external examination; field determination; slit-lamp examination, with observation of the vitreous, and indirect ophthalmoscopy, with and without scleral pressure. The retina was usually observed by more than one person. Localization was made by drawings, with consideration of the meridian, site of the breaks, and relation to the vascular geography. Observations during surgery was made similarly.

Despite well-recorded case histories, certain findings were missing among the records or were difficult to ascertain. Thus, in the subsequent analysis, the number

TABLE 3.—*Incidence of Success in All Cases*

	No. Cases	Per Cent
Successes	316/618	51
Successes (excluding 9 failures in patients refusing reoperation)	316/609	51
Successes (including those without 6-mo. follow-up)	381/618	62

TABLE 4.—*Influence of Preoperative Findings in All Groups of Refractive Errors*

	No. Cases	Per Cent Success
Macula attached	104	85
Macula detached	303	64
Fixed folds	55	50
Lattice degeneration	40	80

of cases vary. All findings, however, are derived from among the 451 cases, in 316 of which the retina has been reattached for six months and in 135 of which the result was a failure.

ANALYSIS OF DATA

It is attempted to establish which preoperative findings and which operative techniques influence reattachment of the retina. Some of the factors presented are significant. However, many others are not. Significance is established when the probability of error is found to be 5% or less. The following factors have been demonstrated to be significant by this method of analysis.

Condition of Macula.—Of cases in which the macular area was not detached, the result was successful in 85%, whereas of those with detachment of the macular area, success was obtained in only 64% (Table 4). Thus, in cases with detachment of the macula before operation the prognosis was poorer than in those with attachment.

Preoperative Fixed Folds.—Reattachment was less successful in eyes with fixed folds before operation than it was in the whole operative group (Table 4).

Area of Detachment.—It was found that in cases with total detachment of the retina the prognosis was poorer than in cases in which one or less than one quadrant was detached. In only 40% of the cases with total detachment was the operation successful, whereas, in all 20 eyes with less than one quadrant detached the operation was successful (Table 5). Of all the cases in which operation was successful, there was detachment of the retina before operation in only 13%.

TABLE 5.—*Retinal Area Detached Before Operation (406 Eyes)*

Quadrant	No. Eyes	Per Cent Success
Local (less than one)	20	100
One	100	60
Two	158	79
Three	63	64
Four	95	40

TABLE 6.—*Number of Breaks Found Preoperatively*

	No. Cases	Per Cent Success
None	13	53
One	134	84
Two or more	285	65

TABLE 7.—*Successful Operations Within Refractive Error Groups*

	No. Cases	Per Cent Success
Aphakia	84	50
Myopia*	101	72
Emmetropia hyperopia	186	84
Unrecorded	80	56

* Greater than 3 D.

TABLE 8.—*Influence of Preoperative Findings in Cases of Aphakia*

	No. Cases	Per Cent Success
Aphakia	84	50
Intracapsular	72	53
Extracapsular	12	33
Fixed folds	26	23

Number of Breaks.—It is noted that the number of breaks may be many more than two. They were recorded as two or more, however, to simplify the analysis. When no break was found, or when two or more breaks were found, the prognosis was poor. The prognosis was better if only one break was found (Table 6).

Aphakia.—Among the refraction groups, treatment was significantly less successful in the aphakic eyes than in all the eyes operated on considered together. A poorer prognosis was associated with the presence of fixed folds in aphakic eyes (Table 7). Of the aphakic eyes without fixed folds, the result was successful in 66%.

The following factors could not be shown to be significant.

Extracapsular Extraction.—An analysis of the aphakic group did not indicate that the difference in percentages of success between the group undergoing extracapsular extraction and the group undergoing intracapsular extraction was significant (Table 3). Analysis was made within the group in relation to each other. However, the probability of error did approach 5%. Perhaps when a

TABLE 9.—*Examination of Ora Serrata*

	No. Cases	Per Cent Success
Ora serrata examined	335	76
Ora serrata not examined	61	66

TABLE 10.—*Age Groups of Patients Operated on*

	No. Cases	Per Cent Success
>60	149	68
<60	274	71
>50	256	70
<50	167	70

TABLE 11.—*Diathermy Treatment of Breaks (464)*

	No. Times Used	Per Cent Success
Breaks alone	44	77
Breaks plus barrage	289	70
Barrage alone	131	66

TABLE 12.—*Methods of Fluid Release at Operation*

	Times Used	Per Cent
No perforation	55	91
Walker pins	52	67
Diathermy point	80	62
Incision of sclera with needle point; perforation of choroid	814	61

larger group of cases of extracapsular extraction can be included, the factor will be found to be significant.

Examination of Ora Serrata.—A comparison could not be made between cases in which the ora serrata was examined and those in which it was not examined. The group recorded as cases in which the "ora serrata not examined" was too small. Moreover, the decision to examine the ora serrata was determined by the findings in the rest of the detached retina.

Lattice-like Degeneration of Retina.—In these cases the prognosis was not poor (Table 4).

Age.—Age did not affect the prognosis when considered for patients above and below 60 years of age and above and below 50 years of age.

Variations in Operative Technique.—The influence of various factors in the operative techniques was considered. Especially, however, were we concerned with the treatment of breaks (Table 11) and the method of fluid release (Table 12).

In almost all cases the operative technique consisted of surface diathermy applied (1) to cover the breaks; (2) to cover the breaks, and also to wall off the area by extension of diathermy to the ora serrata from either side of the breaks, or (3) when breaks were numerous over a large area, to wall them off from the central retina by extending several rows of diathermy around them, but not over each break. No statistical significance could be established when these three groups were considered. The probability of error was greater than 5%. However, the results suggest that success is more frequent when the breaks are covered.

The analysis of the presented group did not indicate that one method of releasing subretinal fluid was better than another. However, oftenest the fluid release was by incision of the sclera, with perforation of the bared choroid by a fine diathermy point. When it was not necessary to release fluid, the prognosis was better.

TABLE 13.—*Incidence of Some Preoperative Findings (451 Cases)*

	Per Cent
Demarcation lines	8
Lens opacities	19
Preoperative vitreous hemorrhage	12
Retina in other eye	
Detached	27
Not detached	38

Although not analyzed, complications were sometimes encountered during fluid release. These consisted of vitreous loss, vitreous hemorrhage, retinal perforation, and retinal prolapse. The last-mentioned complication occurred after incision of the sclera and perforation of the choroid, while the intraocular tension was elevated excessively.

Relation of Preoperative Findings to Detachment.—The incidence of some preoperative findings was of interest (Table 13).

Demarcation lines were present in 8% of the 451 cases.

Lens opacities were recorded only with regard to opacities in the posterior cortex. Opacities present elsewhere are difficult to interpret as abnormal after middle age. Indeed, beginning changes in the posterior cortex may be observed or overlooked by different observers. It would seem that the incidence of opacities of the posterior cortex is at least 19%.

Vitreous hemorrhage occurring with retinal breaks and detachment is probably commoner than the 12% noted. This figure, however, was derived by the objective observance of blood or blood remnants in the vitreous, or near the ora serrata. Probably many more cases were missed because of the time interval between onset and examination; therefore, it is probably commoner than is indicated.

Every ophthalmologist is alert to the finding of detachment in the patient's good eye. The observation of detachment in 27% of the fellow eyes among patients

in this group is, again, probably low. The figure is based on the total number of cases rather than on cases in which the second eye was examined.

It is noted than when the cases are grouped according to errors of refraction, 59% of the myopes had detachments before the age of 50 (Table 14). This is consistent with the belief that detachments occur among myopes at an early age.

SUMMARY AND CONCLUSIONS

Six hundred eighteen cases of idiopathic detachment of the retina are presented. Operation was performed in 525 cases. Operation was successful in 70% of the cases in which it was performed. When follow-up observation is continued, this figure may be raised to 74%. When all cases are considered, therapy was successful in from 51 to 57%. When follow-up study is continued, this may be raised to 62%.

Preoperative findings which were found to affect the prognosis for retinal reattachment are presented. The prognosis was poorer when there was (1) detachment of the macula; (2) fixed folds of the retina; (3) total detachment of the retina; (4) no break or two or more breaks, or (5) aphakia with fixed folds.

TABLE 14.—*Refractive Error Among Patients Less Than 50 Years of Age*

	Total No.	Per Cent Less Than 50 Yr. Old
Myopia*	99	59
Aphakia	81	15
Emmetropia hyperopia	167	36
Unknown	74	43

* Greater than 3 D.

Other preoperative findings were not shown to affect the prognosis. These were (1) the extracapsular type of cataract extraction; (2) failure to examine the ora serrata; (3) lattice-like degeneration, and (4) age. However, analyses of the results suggest that the first factors would have been significant had the number of cases been larger.

Variations in the operative techniques used could not be demonstrated to affect the therapeutic result; these were (1) the method used to treat the breaks, and (2) the method used to release subretinal fluid.

It was noted that the prognosis was better when it was not necessary to release subretinal fluid.

Preoperative hemorrhage occurred in at least one-tenth of the cases.

The retina in the fellow eye was detached in 27% of the cases.

Myopic patients tend to have detachments of the retina at an earlier age than do patients with other refractive errors.

ABSTRACT OF DISCUSSION

DR. CHARLES L. SCHEPENS, Boston: There is no doubt that the statistical method is inadequate for investigating polymorphous cases, such as those of retinal detachments. Statistics of the kind presented are useful, however, as they show an effort toward attainment of more objectivity. The greatest difficulty is that most of the statistics already published are not comparable. The authors of this paper have chosen a very simple basis for comparison: They have included all patients with

retinal detachment examined at the retina service, even though a number of them were unfit for surgery. But even though this reference line was accepted for all similar statistical analyses, another factor renders comparison difficult. Those of you who see a large number of cases of retinal detachment will probably agree that as years go by your results get worse, because more and more of the complicated cases are referred to you. At the retina service of the Massachusetts Eye and Ear Infirmary, complicated cases also become more numerous each year. As an example, it may be noted that the large percentage of cases with aphakia (18%) still seems to be on the increase for 1952.

It is easy, therefore, to understand why the proportion of good results is relatively low (57%). If this material were treated in the way most statistics are formed, the percentage would rise to 74.

I am glad that the visual acuity was not taken into consideration in this presentation, because it is so difficult to choose a good basis for comparison. It would be fair to compare the best postoperative vision with the visual acuity just before the detachment occurred, but the latter is very often not on record. A substitute is a comparison of the best postoperative vision with the preoperative vision, but before operation the acuity is often extremely variable. For instance, a large balloon may overhang the macular region, reducing vision to counting of fingers, but the acuity may rise to 20/40 or better after bed rest.

The authors deserve credit for bringing out two extremely significant points: (1) the importance of early diagnosis, when the detachment is still localized and shows no fixed folds, and (2) the importance of examining the fellow, and apparently healthy, eye. In one out of three or four cases the fellow eye shows either retinal breaks or a beginning retinal detachment.

Dr. Peter C. Kronfeld, Chicago: The principal value of this statistical study lies in the fact that it gives one an over-all picture of the results of surgical treatment of idiopathic retinal detachments. The ophthalmologist, grappling with a few cases of detachment at a time, has difficulty in getting an over-all picture and in remembering it. He therefore will find this paper helpful and, at the same time, reassuring.

The statistical approach used here—and I believe the authors deserve a great deal of credit for using it cautiously—provides a basis for comparison of different series, and it is only natural for me to compare this new series with the series which Dr. William F. Hughes Jr. presented in the symposium on retinal detachment at the Academy meeting in 1951.

Analysis of the two series reveals a very high degree of parallelism with regard to percentage of successes, as well as with regard to those factors that seem to be of prognostic significance. It may be worth while here to point out the few differences between the two series.

Dr. Smith and Dr. Pierce draw a fairly sharp line between cases with one break and cases with two or more breaks in the retina. Dr. Hughes, in his statistical analysis, failed to find such a difference; nor does my personal experience point in that direction. One giant tear is infinitely more difficult to repair than two average-sized tears. However, considering just average-sized, horseshoe-shaped tears, I am not certain of any significant difference in prognosis between cases with one tear and cases with two tears as long as the two tears or breaks are located in the same quadrant.

I believe that the extent of atrophying, and eventually break-producing, retinal disease has a great deal to do with the prognosis. Unfortunately, the extent of this atrophying disease is difficult to assess. The extent is exaggerated as long as the retina is detached, and it is minimized the moment the retina goes back into its normal position.

The number and size of tears are undoubtedly important factors, but I doubt whether the most suitable division line between the more favorable and the less

favorable cases is where Dr. Smith and Dr. Pierce have put it, that is, between one and two tears.

Personally, I am not in a position to suggest a better formula. Any mathematical formula would have to consider size, number, and location of those tears, and to put these factors into any kind of formula would be very difficult.

I was sorry not to find in this analysis reference to the prognostic value of the settling down of the retina on immobilization prior to the operation, and also to the settling down that occurs during the operation. I think it is a very important prognostic factor, and one that was very clearly brought out by Dr. Hughes in the statistical analysis presented at the last Academy meeting.

Between the lines of this paper I read a feeling of apprehension on the part of the authors over very extensive coagulations made necessary by the extent of the pathological process in some of their cases. I share with them this feeling of apprehension. It is important to realize that high frequency currents entail undesirable effects upon the vitreous should the vitreous still be there, and also upon the retina. It is important to realize that bipolar application of galvanic current offers an opportunity for more localized and milder, more circumscribed coagulation.

While this paper deals primarily with the statistical aspects of idiopathic detachment, I cannot suppress the following statement: In a certain number of cases the treatment as used by the authors and the various attending men at the Massachusetts Eye and Ear Infirmary failed to bring about a state of reattachment. It is my feeling that in some of these cases immeasurable benefit might have been derived from a scleral resection operation.

BLEPHAROPTOSIS TREATED BY THE FRIEDENWALD-GUYTON SUTURE

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AND
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HONOLULU, T. H.

CORRECTION of ptosis by a single, buried, permanent suture anchoring the lid to the frontalis muscle was originally described by Friedenwald and Guyton in 1948.[1] Because, to our knowledge, nothing has appeared in the literature on this subject since that time, it is considered worth while to evaluate the results in a series of 35 cases of blepharoptosis treated by this method.

TECHNIQUE

The technique, as described by Friedenwald and Guyton, is as follows: Two small stab incisions are made at the upper border of the brow, one 5 mm. lateral to the nasal termination of the brow and the other approximately 3 cm. lateral to the first. Each incision is made down to the periosteum. Two tiny incisions are then made through the skin of the upper lid, 2 mm. above the lid margin and about 2 cm. apart, placed symmetrically so that they lie about 7 mm. from the nasal and lateral canthus, respectively. A braided white nonabsorbable surgical (silk) suture (size 00 to 2) on a No. 5 ⅜-circle cutting needle is passed into the medial of the two incisions above the eyebrow, through the fascial termination of the frontalis muscle (just over the periosteum), and out through the lateral eyebrow incision. From here the suture is carried downward beneath the skin and the orbicularis muscle of the upper lid to emerge through the lateral lid incision. The suture is then passed through the dermis 2 mm. from the lid margin, parallel to the lid margin and emerging through the medial lid incision, and then upward beneath the orbicularis, emerging through the medial eyebrow incision, where the suture first entered. Here the suture is pulled tight enough to elevate the upper lid 2 mm. above the desired final position and then tied in the depths of the incision. *D* of the Figure shows the immediate overcorrection of the ptosis. Insertion of the suture may be facilitated by the use of a Reverdin needle, as shown in *B* and *C*. We have been pleased with the technical ease encountered[2] in placing the suture with a Berbecker Size 8 surgeon's needle (Fig. 41[3]). Use of this ski-shaped needle is particularly advantageous in traversing the tissues near the lid margin (Fig. *A*). We have found that the needle described by Friedenwald and Guyton offers technical difficulties because its rounded curve is not in alignment with the desired suture tract. Although the shape and mechanical advantages of the Reverdin needle are desirable, it passes with much more resistance than the ski-shaped surgical needle.

It has been emphasized[1] that the horizontal leg of the suture tract above the lid margin should traverse the corium of the overlying skin. As an alternative, the suture may pick up the superficial fixed tissues of the tarsus. Failure of ptosis correction will follow if the suture passes merely through the loose integument between the skin and the tarsus.

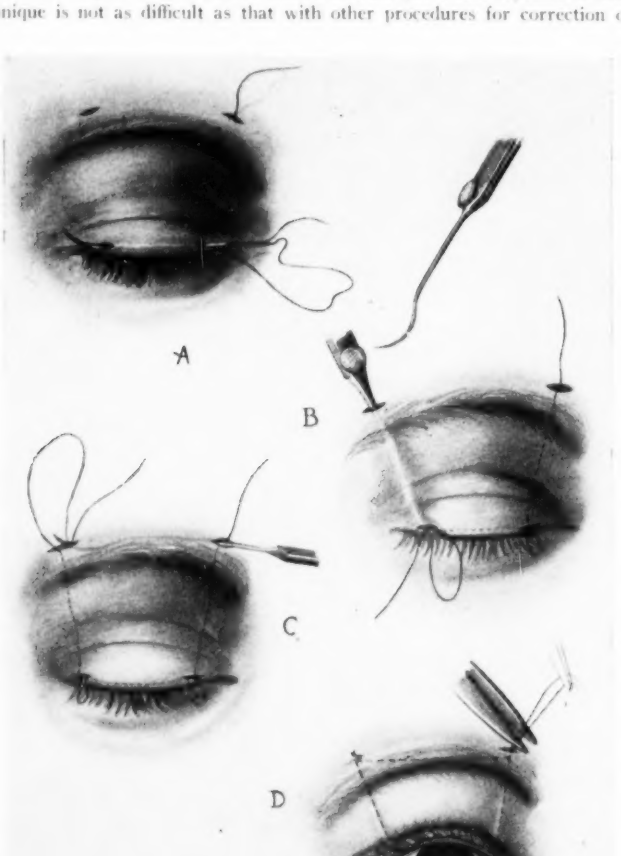
1. Friedenwald, J. S., and Guyton, J. S.: Simple Ptosis Operation: Utilization of the Frontalis by Means of a Single Rhomboid Shaped Suture, Am. J. Ophth. **31**:411-414 1948.

2. Constantine, F.: Personal communication to the authors.

3. Julius Berbecker & Sons, Inc., New York.

If the horizontal leg of the suture above the brow is not deep enough to traverse the terminal fascia of insertion of the frontalis muscle, the soft tissues will buckle. Later, the correction of the ptosis will fail as the suture cuts into the buckled soft tissues.

The procedure is simple and may be done before, after, or in conjunction with other procedures. The suture may be removed after failure and the placement repeated if necessary. The surgical technique is not as difficult as that with other procedures for correction of blepharo-



Technique of inserting the Friedenwald-Guyton suture for correction of blepharoptosis.

ptosis. For these reasons the method has gained popularity. That the advantages greatly outweigh the disadvantages is demonstrated by the results in the series of cases reviewed. The procedure was successful in 83% of the cases.

SUMMARY OF CASES

During the period from 1946 to 1951, 158 operations for correction of blepharoptosis were performed on 122 patients by various surgeons at the Manhattan Eye, Ear and Throat Hospital and the New York Eye and Ear Infirmary. Procedures

used were as follows: (1) shortening of the levator, 98 operations; (2) attachment to the superior rectus, 12 operations; attachment to the occipitofrontalis, 48 operations. Friedenwald-Guyton sutures were used in 35 of the last group, of which 8 were our cases. The poor results obtained in 6 (17%) of the 35 cases are detailed as follows:

CASE 1.—The suture was inserted for treatment of blepharoptosis in conjunction with blepharophimosis. Severe exposure keratitis followed, necessitating removal of the suture.

CASE 2.—Infection and keloid formation followed operation for congenital ptosis. The suture was removed 4½ months after operation.

CASE 3.—Trichiasis occurred immediately after operation in a patient with a previous tarsal resection. The suture was removed before the patient left the hospital.

CASE 4.—In a patient 3½ years old with bilateral congenital ptosis a wire suture was employed to suspend the right upper lid and a silk suture for the left lid. Both sutures were removed. The silk became infected two months after operation. Two and one-half years later the patient sustained an injury which ruptured the wire suture. The broken wire created a distortion of the overlying tissues in the supratarsal sulcus. Although the sutures had to be removed, the ptosis was greatly improved. The behavior and lack of cooperation of this child may have been factors in the failure of the sutures.

CASE 5.—A young woman complained that after insertion of the suture her eye remained open when she kissed. The suture was removed at her insistence, even though ptosis recurred after its removal. To her, the ptosis was preferable to the aspects of the lagophthalmos.

CASE 6.—On the first postoperative day the suture had to be removed because of a technical error in operative procedure.

Postoperative complications may be summarized as follows: (1) rupture of the suture following a heavy blow on the brow; (2) postoperative trichiasis; (3) limitation of motion of the eyelid and exposure keratitis resulting from an error in placement of the suture; (4) early and late infections around the suture.

The possibility must be considered that the number of complications in this series is greater than would have occurred if the series of operations had been done by one surgeon using the same technique.

COMMENT

Correction [4] of blepharoptosis by shortening the levator muscle is preferable to operations that substitute use of the superior rectus or occipitofrontalis muscle for levator action because the postoperative anatomy and physiology more closely approach normal. For this reason the Friedenwald-Guyton suture is indicated (1) when other procedures have failed to correct the ptosis; (2) when exposure keratitis coincident to other procedures is feared; (3) when the condition of the levator or superior rectus cannot be determined; (4) when there is acquired ptosis due to paralysis of the levator; (5) when a temporary means of correcting bilateral ptosis in early childhood is desired, thereby gaining time for growth and cooperation; (6) when the Marcus Gunn, or jaw-winking, syndrome is present, with or without levator excision; (7) when a test of corneal tolerance to exposure is desired before an irreversible procedure is contemplated; (8) when correction of blepharoptosis is to be done by one not experienced in ptosis surgery.

4. Burke, R.: A Simplified Blascovics Operation for Blepharoptosis, Tr. Am. Ophth. Soc. **49**:297-350, 1952.

The Friedenwald-Guyton technique should be carried out with the patient under general anesthesia because the local edema of infiltration anesthesia obscures landmarks. A variation in technique, employed by Gailey,[5] permits use of infiltration anesthesia but necessitates use of a wire suture. The ends of the wire are twisted instead of tied and are left to emerge through the initial brow incision. After the edema has subsided, the wire is adjusted by further twisting and is cut beneath the skin surface. The wound is then closed. Although it appears that this procedure might invite infection into the suture tract, Gailey claims that the incidence of infections is not increased by this method. It is our feeling that tantalum wire is not as desirable as silk, cotton, or nylon as suture material because it is more subject to breakage and fragmentation from trauma than are substances of greater flexibility. Stainless steel wire is undesirable because the large-caliber wire necessary to maintain the position of the lid causes excessive rigidity and surface deformity. A new stainless steel wire (size 00000, Davis & Geck, Inc.) may offer some promise, but we have had no experience with it as yet.

SUMMARY

Results are evaluated in a series of 35 cases of blepharoptosis treated by the Friedenwald-Guyton suture method. The operations were done at two hospitals by numerous surgeons. Favorable results are reported in 83% of the cases. Technical details and reasons for failure are enumerated.

The Manhattan Eye, Ear and Throat Hospital and the New York Eye and Ear Infirmary cooperated in this study.

5. Gailey, W.: Personal communication to the authors.

SURGICAL ASPECTS OF DEFECTIVE ABDUCTION

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DEFECTIVE abduction is the result of various conditions having little in common other than a limitation in abduction. For this reason, it is evident that these various conditions are nonconcomitant. They have therefore few, if any, of the various causes of concomitant strabismus. In all cases the defective abduction is the result of a peripheral orbital defect, i. e., neuromuscular, of the muscle alone, or of the muscle and the fascia, or is due to a pathological condition of the central nervous system, i. e., congenital (perhaps developmental), disease of the central nervous system, trauma, or neoplasm. Three of the defects to be considered are usually spoken of as congenital. These are the Duane retraction syndrome, strabismus fixus, and so-called congenital sixth nerve paralysis. A fourth, to be discussed, is an acquired, or permanent, form of sixth nerve paralysis.

THE RETRACTION SYNDROME

The retraction syndrome is an interesting syndrome, or group of signs, about which there is an amazing amount of misinformation not only as to the pathological changes, but also as to the surgical procedures which have been recommended for its improvement at various times by various persons. When its pathological anatomy is understood, one can see why it is absurd to recommend, for example, the use of muscle-tendon transplants from the superior and inferior rectus muscles for correction. There is little wonder that this valuable procedure has been discredited by some ophthalmologists when utilized so improperly.

The retraction syndrome is an oculomotor condition of limited abduction in which the eyeball when abducted as much as is possible in the individual case manifests some degree of exophthalmos. When adduction is carried out *ad maximum*, enophthalmos occurs, and this is accompanied by pseudoptosis of the upper lid. There is no impairment of levator muscle function. The ptosis results from some posteroward traction upon the eyelid and from a lessened support of the eyeball for the upper eyelid, both by reason of the enophthalmos. This condition is the exact opposite of the widening of the palpebral fissure which appears with the abduction effort as a result of the exophthalmos. Neither conjecture nor conclusions from the surgical exploration of the orbit in these cases disclose any other possibility. In addition, there is an overaction of the superior and inferior oblique muscles in the fields of their maximum vertical action. The fields of maximal ver-

From the Wills Hospital.

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tical action of the superior and inferior rectus muscles show no constant or characteristic change. There is not uncommonly, however, a definite limitation in the vertical action of these muscles, certainly as compared with the vertical action of the oblique muscles, and also as compared with the maximal vertical action of the

Fig. 1.—Unilateral retraction syndrome simulating divergent strabismus. Adduction limitation is actually greater than abduction limitation. Other classic characteristics of retraction syndrome are present.

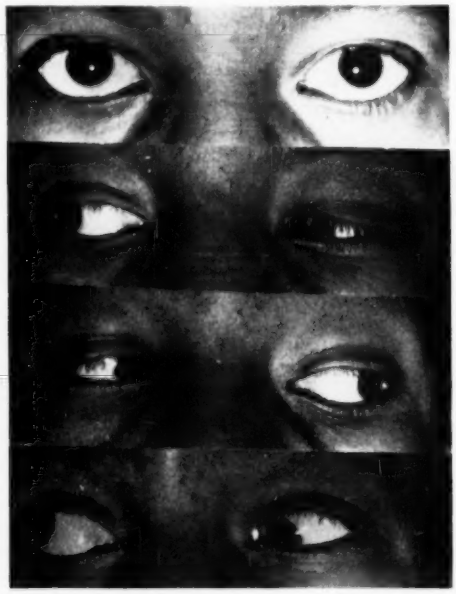

Fig. 2.—Bilateral retraction syndrome. The amount of abduction limitation is negligible as compared with the exophthalmos and enophthalmos. There is no manifest deviation in repose.

normally acting superior and inferior rectus muscles of the opposite eye. The pathological anatomy can account for this. The retraction syndrome is usually a unilateral defect, although slight to moderate degrees of bilateral involvement have been seen, though rarely. Figure 1 represents a unilateral case, and Figure 2 a bilateral case, of this condition.

While abduction is limited, or even nil, involvement of adduction, though less limited than the impairment of abduction, may be present as well, and extreme instances have been reported in which adduction was more limited than abduction. Figure 1 illustrates this. Cases of this type will simulate a divergent strabismus. Cases of the commoner type will simulate a convergent strabismus.

Amblyopia from suppression is relatively uncommon, though it may be present to a marked degree. Torticollis is common, and in those cases with a pronounced limitation of abduction there is frequently a compensatory head facing to escape diplopia. It is natural that one or the other should be present: a head tilt and compensatory facing or suppression with amblyopia.

These conditions should not be spoken of as oculomotor paralyses. The limitation in abduction and/or adduction is a structural muscular and fascial change, both gross and microscopic in type, and is not necessarily due to a sixth nerve paralysis. All degrees of involvement are seen, depending upon the degree of fibrosis of muscle and fascia present. Figure 3 illustrates diagrammatically the

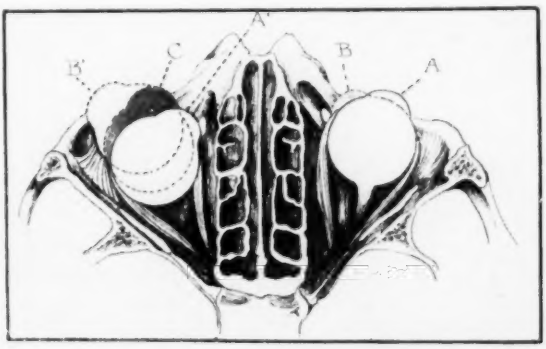

Fig. 3.—Basic pathological mechanism of the retraction syndrome: *A* and *B*, right eye, normal abduction and adduction; *A'* and *B'*, left eye, enophthalmos and exophthalmos characteristic of the syndrome due to fascial defect of the external rectus muscle; *C*, the normal.

faulty anatomy and the effects of this in lateral movements. The right eye illustrates abduction and adduction, as seen in *A* and *B*, without any significant change in the position of the center of rotation of the eyeball within the orbit.[1] The left eye is drawn diagrammatically to illustrate a retraction syndrome. The fault is depicted as a fan of adhesions limiting the amplitude of action of the external rectus muscle. No great liberty is being taken here, either editorial or anatomical. This diagram illustrates not an oculomotor paralysis but a limitation in the amplitude of abduction, combined with partial fixation of the eyeball, so that the center of rotation of the globe itself and the position of this within the orbit have both been displaced laterally. This situation is demonstrated when one attempts passive movements of the eyeball with a pair of forceps, with the patient under general anesthesia. One may demonstrate this actual fixation of the globe by grasping the eyeball over the external rectus muscle with such forceps; one usually has the feel

1. It is well known that there is an actual change in this position, but this is not sufficient in extent to be relevant to the explanation.

or impression of an inelastic or a fixed external check ligament. (It is well to review Whitnall's classic discussion [2] of the fascia of the orbit at this time.)

Maximum abduction under such anatomical circumstances, even if achieved only by reciprocal denervation of the adductors, must be accompanied by exophthalmos, as illustrated in *B'*. Adduction, whether limited or not, as seen in *A'*, will result in a posteroward displacement of the globe into the orbit because of this eccentric fixation of the globe in the orbit and/or to the periorbita.

The abnormalities of the vertical movements of the two oblique muscles are illustrated in *B* of Figure 3. *A*, of Figure 4, the normal, shows the line of maximum vertical effect of, for instance, a superior oblique muscle. When the globe is adducted and simultaneously displaced posteroward, as in *A'*, the scleral insertion of an oblique-muscle tendon is also displaced posteroward, though without any change in its exact position upon the globe itself. This results in more effective vertical action of the oblique muscles under such circumstances, hence a pronounced true overaction. The same mechanical effect can be seen in traumatic

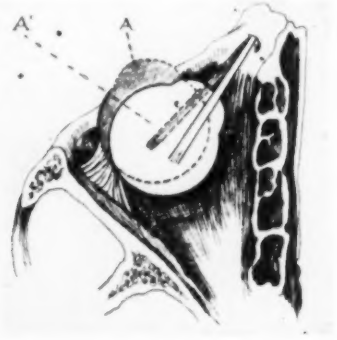

Fig. 4.—Drawing illustrating the reason for overaction in the field of the oblique muscles: shaded muscle and eyeball (*A*), the normal; unshaded muscle and eyeball, *A'*, in enophthalmos, hence more effective vertical action.

conditions in which enophthalmos is present because of a fracture of the floor of the orbit.

Figure 5A is a drawing, front view, illustrating the retraction syndrome: the upper, showing no manifest lateral deviation; the middle, homolateral abduction, i. e., abduction toward the involved side, illustrating the exophthalmos as well as the limited abduction, and the lower, contralateral adduction, with enophthalmos and pseudoptosis. Figure 5B shows the overaction in the vertical action of the oblique muscles. The head tilt so commonly present in these cases suggests—in fact, proves—that in this syndrome there is a rotational overaction of the oblique muscles as well.

Considering this anatomical relation, it is easy to see that any type of tendon transplantation is wholly out of the question. Surgery, under the best of circumstances, can only (*a*) correct the manifest ocular deviation, (*b*) minimize the faulty

2. Whitnall, S. E.: Anatomy of the Human Orbit and Accessory Organs of Vision, Ed. 2, London, Oxford University Press, 1932.

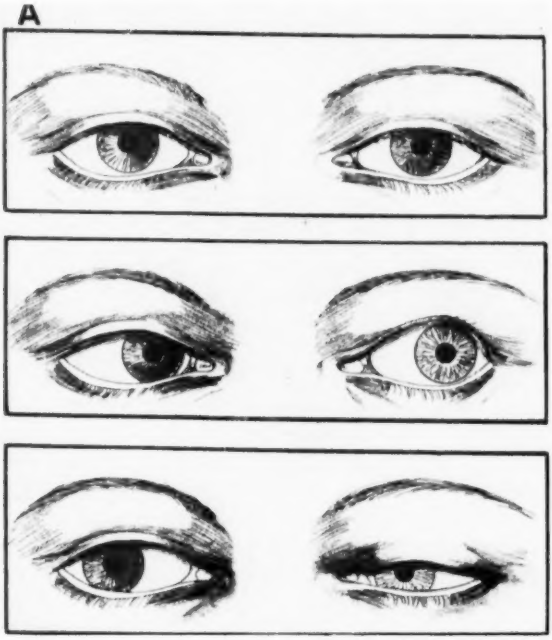

Fig. 5A.—Drawings showing the retraction syndrome, front view: upper part, no manifest lateral deviation; middle part, exophthalmos; lower part, enophthalmos with pseudoptosis.

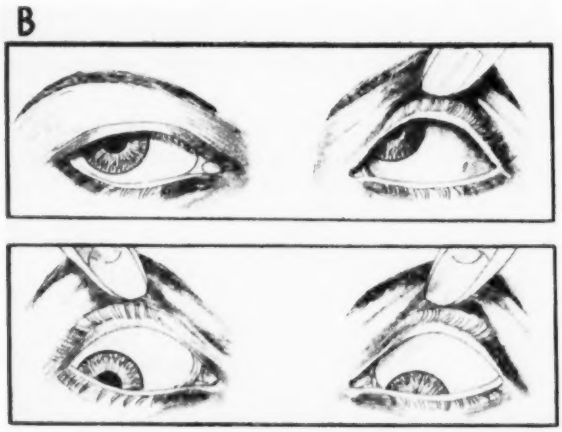

Fig. 5B.—Overaction in the field of greatest vertical action of the oblique muscles.

facing and head tilt, and (*c*) perhaps, reduce the deformity of exophthalmos and globe retraction. It is essentially surgery for cosmetic reasons, with a hope of obtaining single binocular vision in the midline. A recession of the medial rectus muscle is first to be considered and is the first procedure to be carried out. This may limit the retraction of the eyeball, will correct a manifest convergence deviation, and may also correct faulty facing. Next, the external rectus muscle should be explored surgically for the resection of pathological fascial bands, for the release of a hypertrophied external check ligament, and for the resection of the external rectus muscle, if that is indicated or necessary.

Lyle and Cross,[3] in discussing the surgery of the oculomotor paralyses, also called attention to the inadvisability of any muscle transplantation in this condition. Their statement is that it is "never indicated."

Surgery of the superior and inferior oblique muscles is rarely indicated. The results of such intervention, at the best, are usually disappointing, though frequently it seems that a recession of the inferior oblique muscle should be done. The procedure can do no harm; frequently it will do no good. In this consideration one should be guided by the degree of fusion present, the presence of amblyopia, and the presence or absence of torticollis from overaction of the inferior oblique muscles. This definitely modifies the patient's ability to develop single binocular vision. Tenotomy of the superior oblique muscle should be done seldom, if ever. It is most important to remember that the function of downward gaze is far more important to the human than is that of upward gaze.

STRABISMUS FIXUS

Strabismus fixus may be considered as a variant of the retraction syndrome, due to anatomical changes slightly different, perhaps, but essentially similar in effect, to limit abduction. In this condition one finds a rigid, fibrosed medial rectus muscle attached by a broad insertion to the sclera. This insertion is pathologically widened not only circumferentially but also anteroposteriorly. Such an attachment is occasionally seen to exist far posteriorly, even behind the equator of the globe. Naturally, abduction is wholly nil.

In Figure 6, the upper portion is a front-view drawing of eyes in such a case of strabismus fixus. The lower portion illustrates the manner in which the child must view the contralateral field, using free rotations of the head. The left field is seen with the right eye, and the right field is seen with the left eye, assuming that the situation is bilateral. Unilateral strabismus fixus is the commoner, but bilateral strabismus fixus is not as rare as is the bilateral retraction syndrome.

Figure 7 illustrates either a case of bilateral strabismus fixus in which the left eye has been operated on or a case of unilateral strabismus fixus in the right eye with consequent crossed diplopia. The drawing suggests a pathological internal rectus muscle on the right and either a normal internal rectus muscle or a recessed pathological muscle on the left. The diplopia as outlined in such an instance is easily understood.

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3. Lyle, T. K., and Cross, A. G.: Diagnosis and Management Paralysis of the Extrinsic Ocular Muscles, with Special Reference to Surgical Treatment in 219 Cases, Brit. J. Ophth. **35**:511, 1951.

Fig. 6.—Strabismus fixus. Below is illustrated the manner in which the child must view the left and right fields with the contralateral eye, using free rotations of the head. A light reflex in the right pupil is the result of a light source from the left. A light reflex on the left eye is on the temporal conjunctiva-sclera.

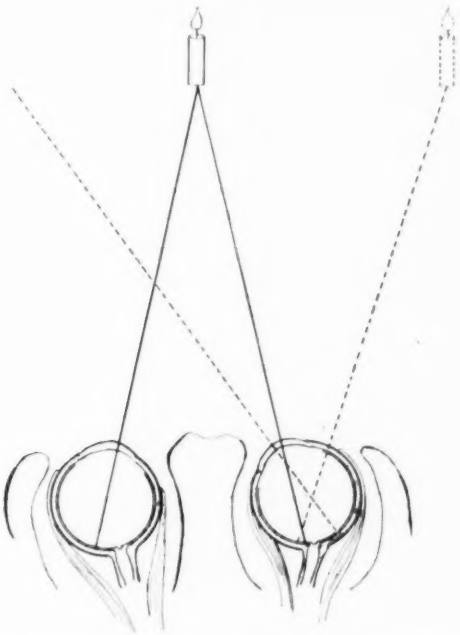

Fig. 7.—Elementary drawing emphasizing not the simple physiological aspects of strabismus-fixus diplopia but the necessity for alternate suppression, as well as the difference between this condition and abduction limitation due to paralysis of the external rectus muscle. See text.

The surgical procedure in this condition is relatively simple in principle, though frequently difficult to perform because of the mechanical conditions present. It is wise to state here that rupture of the sclera has occurred during the surgical procedure in such situations by overenthusiastic tugging upon the fibrosed muscle with a muscle hook in the attempt to isolate the medial rectus muscle.

One must do a free recession of the fibrosed internal rectus muscle, in an amount sufficient to obtain maximum results—perhaps better expressed as an optimum cosmetic appearance. One may substitute limited adduction for the pronounced convergent strabismus without increasing to any great extent the abduction ability of the eyeball. Single binocular vision is seldom, if ever, present in cases of bilateral strabismus fixus. It is almost impossible for this to occur. In unilateral strabismus fixus, if amphlyopia is not present, the patient will achieve single binocular vision by utilizing free rotations of the head to obtain parallel visual axes. White did not hesitate to do a free tenotomy on the internal rectus muscle in many instances, for the fibrous bands can be too extensive for any other procedure.

CONGENITAL SIXTH NERVE PARALYSIS

So-called congenital sixth nerve paralysis is probably the commonest of the congenital ophthalmoplegias. In such cases there may be a marked manifest bilateral or unilateral convergent strabismus. Even in bilateral cases the situation may seem to be only unilateral because of an ability to fix with one eye in the midline while the other (if the condition is bilateral) is in secondary deviation. The condition is more commonly unilateral, and the defect may appear only in attempted lateral rotation. In unilateral cases and in cases with a marked dissimilarity in the degrees of involvement a postural compensatory rotation of the head, to escape diplopia, is very frequently seen.

In Figure 8 are drawings in a case of bilateral involvement. In the upper drawing the eyes seem to have no manifest deviation; in the middle and the lower ones, however, lateral rotations to the right and to the left illustrate the abduction defect.

Figure 9 is a drawing in a case of monocular involvement with a manifest deviation in which the child demonstrates his desire for single binocular vision by the rotation of the head toward the field of the paralyzed muscle.

The etiology in cases of this defect is very much in doubt. It does not seem proper to speak of the condition as sixth nerve paralysis because in so many cases remarkable degrees of abduction develop, even to a normal amount, after early surgical intervention. The operation should be carried out as soon as the diagnosis can be made—certainly, if possible, before the second year of life.[4] Cases will be seen repeatedly, of both the bilateral and the unilateral type, in which there is complete absence of abduction and still the visual axes are parallel in the primary position. There is a reasonable doubt whether surgery is indicated in these instances. Too frequently, operation to increase the power of abduction in an affected eye may result in defective adduction in that same eye. It must be remembered, also, in all the various types of defective abduction covered in this paper that, while they are

4. McLean believes that operation can be done in many cases during the first year of life, as soon as one is certain of the situation.

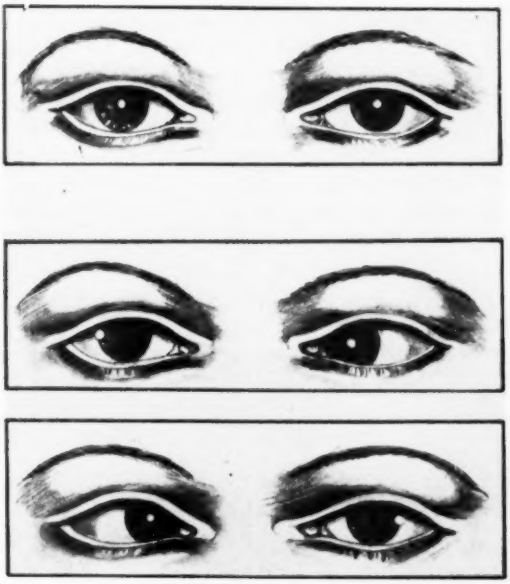

Fig. 8.—Drawings in a case of bilateral sixth nerve paralysis, of congenital type: upper drawing, no manifest deviation; middle drawing, limitation in abduction to the right in the right eye; lower drawing, limitation in abduction to the left in the left eye. Note position of the light reflexes in the pupils.

Fig. 9.—Drawings of monocular involvement in which the child demonstrates his desire for single binocular vision by rotation of the head toward the left, compensatory facing.

nonconcomitant, it is still a mistake to attempt to overcome, as Lyle and Cross [3] said, "a large angle of deviation by an operation upon one eye only; otherwise there is a grave risk of obtaining an asymmetrical result." The surgeon should not substitute an adduction weakness for an abduction defect. Unilateral, or bilateral, recession of the medial rectus muscle only should be done and the patient then observed for a length of time sufficient for one to be certain that additional spontaneous recovery is not occurring. Tendon transplantation may be carried out then if certain conditions, to be discussed later, are present. If not, a resection of the external rectus muscle is the next logical procedure. One must remember that there is always a likelihood that some degree of diplopia will continue on the affected side, or sides, regardless of the surgical procedure. The ideal result is single binocular vision in the midline with a binocular field of lateral gaze sufficient to permit a span of eye movements adequate for normal reading.

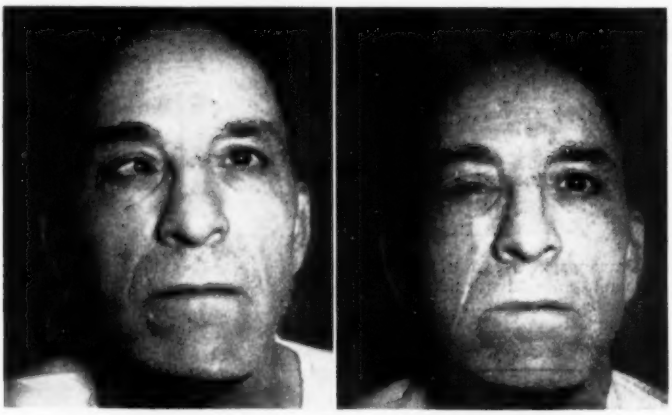

Fig. 10.—Right, acquired, traumatic (fracture of skull) sixth nerve paralysis. Left, end-result of surgical correction. See Figure 15 and text.

ACQUIRED SIXTH NERVE PARALYSIS

Acquired sixth nerve paralysis is the last of the conditions to be discussed (Fig. 10). This may become a surgical problem when it fails to recover spontaneously. Of course, before surgery one should be certain that further spontaneous recovery will not occur. Certainly a postponement of surgical intervention for at least 12 months after the paralysis has occurred, as in a case of trauma to the skull, is a reasonable interval.

The aim of surgery is largely cosmetic in cases in which there is a high degree of deviation, with contracture of the directly antagonistic internal rectus muscle, as seen in cases of long-standing paralyses. Long-standing suppression, when broken up surgically, can result in a most distressing diplopia unless the patient again acquires suppression or has normal retinal correspondence. In general, these paralytic defects should be slightly undercorrected, never overcorrected; an approximation to orthophoria is the ideal.

Acquired external rectus muscle paralysis lends itself beautifully to the use of tendon transplants. There are, however, certain rather rigid factors connected

with the advisability of this operation. In this condition one may always hope for single binocular vision in the midline with a good span of binocular gaze from side to side. A logical sequence of surgical procedures is also to be observed, especially as to the recession of the internal rectus muscle.

If the strabismic eye moves spontaneously to the midline in the bilateral movements of both eyes toward the paralyzed side, one may proceed immediately with the tendon transplantations, combined with resection of the paretic external rectus muscle. One should not do a recession of the internal rectus muscle simultaneously. This is always to be considered as a first-step operation or as a second-stage operation. If the eye does not move spontaneously to the midline, a recession of the internal rectus muscle should be done as a first-stage operation. If the eye then moves to the midline spontaneously, after recovery from this surgical procedure one may proceed with the tendon transplantations. In those cases in which the use of tendon transplants was the first-stage operation, one may find that a recession of the internal rectus muscle will be necessary as a second-stage procedure. In those cases in which the recession of the internal rectus muscle was a first-stage procedure and the tendon transplantation subsequent to that, one may find that a recession of the contralateral internal rectus muscle will be necessary for maximum functional recovery. The use of tendon transplants is not indicated in any other type of case. Recessions and resections are all one can do in such a situation. The end-results of this alternate form of surgical procedures are never very satisfactory in so far as there is any great span of recovery of single binocular vision; and the extensive surgery of tendon transplantation will not help when used in cases in which it is not indicated.

McLean,[5] recognizing this necessity for maintaining the integrity of adduction, treats the internal rectus muscle rather differently. He detaches this muscle, as though a recession were to be done, and then places in the tendon a nonabsorbable loop of suture material to permit later an easy identification of the end of the tendon. The tendon transplantations are then carried out and the conjunctival sutures placed into position. This transplantation portion of the entire procedure is permitted time for complete healing. The detached internal rectus muscle tendon is thereafter reattached as is necessary, according to the circumstances which have developed in adduction or abduction as the result of the transplantations.

The procedure is not to be considered in cases of bilateral sixth nerve paralyses without great deliberation. This warning includes those rather uncommon cases of bilateral sixth nerve paralysis resulting from head injuries or associated with brain-stem lesions, vascular or following craniotomy. It also applies to the congenital cases. In cases of bilateral acquired paralyses one hopes to obtain parallelism at distance without the necessity of prism correction by means of resections of the external rectus muscle tendons with recessions of the internal rectus muscles to an amount necessary for that achievement. The pathological muscle imbalance at near will then need a prism correction in glasses for near vision. In bilateral cases no amount of facing to the right or to the left will permit any breadth of a field for single binocular vision.

In the unilateral cases the judicious use of prisms in a spectacle frame, prisms before one or both eyes base out, or even base out for the paralyzed eye and base

5. McLean made this statement in his discussion of this paper.

in for the opposite eye, in the presence of a slight residual compensatory facing, will frequently correct the facing and permit quite a span in the field of single binocular vision.

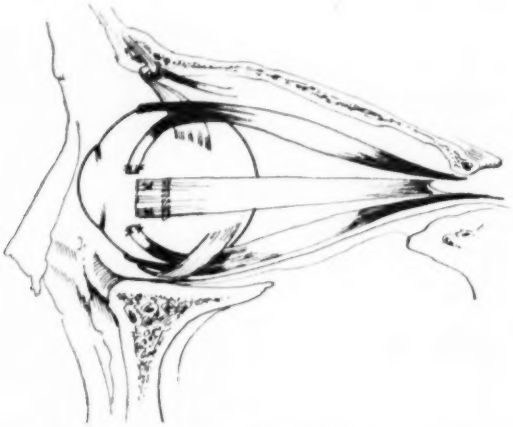

Fig. 11.—Drawing illustrating transplants in position with the advanced and resected external rectus muscle.

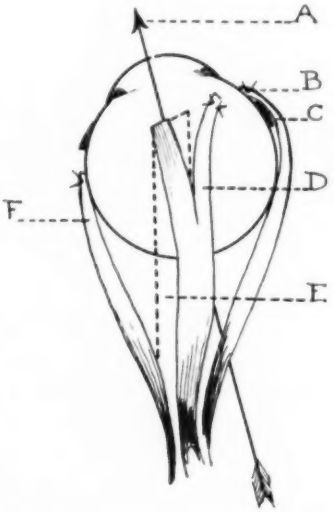

Fig. 12.—Drawing illustrating the completed operation as viewed from above: *A*, anteroposterior axis; *B*, advanced external rectus muscle; *C*, stump of external rectus muscle; *D*, transplanted tendon slip; *E*, original position of superior rectus muscle; *F*, recessed internal rectus muscle. (The scleral attachment of the transplanted slip should lie closer to the advanced external rectus muscle, actually in contact.)

The principles underlying the use of tendon transplants are easily understood. Regardless of the exact technique used for the transplantations, the procedure reduces the amount of adduction by minimizing the adduction ability of the superior

and inferior rectus muscles. This, plus the resection of the paretic external rectus muscle, holds the eye in the midline for the maximum abduction function of the two oblique muscles while working together. The greater the amount of external rotation, the greater is this abduction ability of the two oblique muscles. Adequate adduction, however, must be present. The tendon transplants, brought toward the position of the advanced external rectus muscle, form a fan-like aponeurosis of cicatrix holding the eye in the midline and permitting this abduction function of

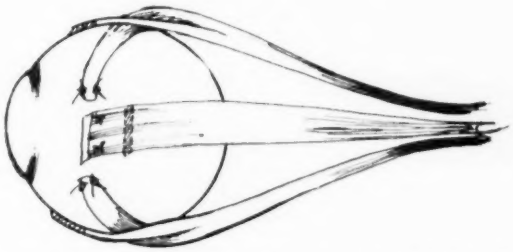

Fig. 13.—Schematic drawing illustrating transplantation of medial slips of muscle, these being passed under the intact lateral slips.

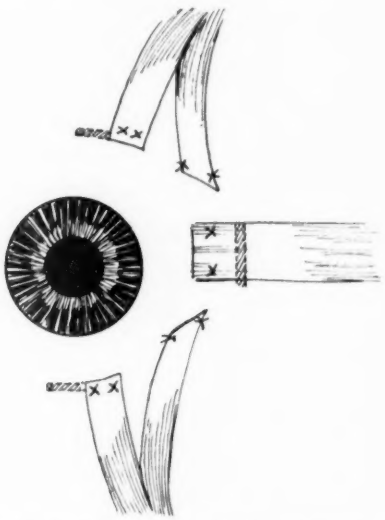

Fig. 14.—Berens' modification of the transplantation, in which the medial slips are transplanted laterally and the lateral slips are transplanted to the position of the advanced and resected external rectus muscle. (The scleral attachment of the transplanted slips should lie closer to the advanced external rectus muscle position, actually in contact.)

the oblique muscles. Certainly, the tendon transplants cannot act as abductors; they can function only as cicatricial adhesions. It is not at all uncommon to find, through this surgical measure, an abduction recovery of 20 to 30 degrees, and even 35 degrees, from the midline lateralward.

Figure 11 is a drawing illustrating the transplants in position as viewed through a conjunctival incision. Figure 12 illustrates the completed operation as viewed

from above and below. The transplant pulls the belly of the rectus muscle lateralward in this development of a sheath of lateral cicatrices. Figure 13 is a modification of the surgical procedure in which the middle portion of the tendon is detached and passed under the intact remaining tendon. Figure 14 is Berens' modification of the transplantation and illustrates complete detachment of the tendon with a lateral displacement of its medial portion to minimize further the total adduction ability of the superior and inferior rectus muscles when functioning simultaneously. Figure 15 shows the completed result in a case with the return of 22 degrees of abduction from the midline.

Fig. 15.—See Figure 10. Left, sixth-nerve paralysis from trauma to the right eye. Right, result of tendon transplantation, with rotations of the right eye bilaterally 28 degrees from the midline without diplopia. The diplopia appeared with rotations greater than that; the amount of abduction recovery, therefore, was more than 20 degrees from the midline.

CONCLUSIONS

In the surgical procedures connected with abduction defects one must first be certain of the underlying pathological process. The surgery can only ameliorate defects. The development of new functions through surgical intervention is not possible. The end-results cannot be the same in all cases of these various conditions; each has an ideal, and this can frequently be approached rather closely. McLean [5] stated the belief that "disappointments connected with . . . procedures are due either to the manner in which the operation has been done or to too much being expected from the procedure." One may add an additional possibility, i. e., that the operation which was performed was done in a case in which it was not indicated.

Ophthalmological Review

THE ELECTRORETINOGRAM

A Review of the Literature

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IT IS WELL known that the vertebrate retina contains three layers of nerve cells: the photoreceptor cells (rods and cones), the bipolar cells, and the ganglion cells, joined to one another in a variety of combinations by cross connections through the horizontal and amacrine cells. The physiologic reactions of the retina are as complicated as is its anatomic structure. The stimulation of the eye by light evokes several types of electric response in the optic nerve, as well as a complex retinal potential made up of at least three easily recognizable components.[1]

The action potential, developed in the retina or in the electroretinogram, has the same properties whether it is recorded between the cornea and the back part of an excised eye or between a differential corneal electrode and an indifferent electrode placed elsewhere on the intact animal. Thus, it is unnecessary to operate around the eyeball of vertebrates in order to apply the electrodes to the eye.[2] In man and other vertebrates one electrode is placed on the sclera or cornea and the other is placed nearby. It may be located on the forehead, on the mastoid process, in the mouth, on the other eye, or in a wound in the skin.[3] The electroretinogram may even be recorded without a corneal electrode, as shown by Motokawa and Mita.[4]

HISTORICAL NOTE

In 1849 DuBois-Reymond first described the resting current between the cornea and the fundus of an eye.[5] Holmgren in 1865 demonstrated that the excised frog eye responded to the onset and cessation of illumination with a positive deflection of a sensitive galvanometer. However, it was not until 1870 that he showed that part of this action current actually originated in the retina.[6] This was independently discovered by Dewar and McKendrick in 1873. Dewar, in 1877, showed that the electric response to illumination could also be obtained from the human eye.[5] Gotch,

Dr. Hermann M. Burian aided in the preparation of the paper.

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1. Granit, R.: Sensory Mechanisms of the Retina, with an Appendix on Electroretinography, London, Oxford University Press, 1947.

2. Hartline, H. K.: Electrical Response to Illumination of the Eye in Intact Animals, Including the Human Subject, and in Decerebrate Preparations, Am. J. Physiol. **73**:600-612, 1925.

3. Karpe, G.: Basis of Clinical Electroretinography, Acta ophth., Supp. 24, 1945.

4. Motokawa, K., and Mita, T.: Über eine einfachere Untersuchungsmethode und Eigenschaften der Aktionsströme der Netzhaut des Menschen, Tohoku J. Exper. Med. **42**:114-133, 1942.

5. (*a*) Granit.[1] (*b*) Karpe.[3]

6. (*a*) Granit.[1] (*b*) Karpe.[3] (*c*) Bernhard, C.: Contributions to the Neurophysiology of the Optic Pathway, Acta physiol. scandinav., Supp. 1, 1940.

in 1903, used a sufficiently fast instrument (the capillary electrometer), and with it he obtained the first electroretinograms, the different phases of which were in agreement with those of the electroretinograms of later investigations.[5]

Kahn and Lowenstein, in 1924, made the first attempt to use the electroretinogram as part of the clinical examination of the human eye but concluded that the practical difficulties of the method made it unsuitable for clinical use.[7] They employed a string galvanometer and leads from the cornea and a distant temporal point on the anesthetized eyeball.[3]

Hartline [2] employed a similar instrument, with greater success. He tried two methods of recording the response: 1. Fluid confined in watertight compartments bathed the eyes. A pair of goggles, equipped with paraffin rims, were molded to fit the face about the eye. Each compartment was filled with sterile saline solution, with which the unpolarizable electrodes made connection. Convex lenses were substituted for the plane glasses of the goggles to make image formation possible. 2. A local cotton-wick electrode made contact with the anesthetized cornea, while the other electrode was placed in the mouth.

Sachs [8] in 1929, recorded the electroretinogram with a gelatin-tipped electrode on the limbus of the anesthetized cornea and the other electrode at the temple. He stated that the only way of correlating the material processes in the receptor organ with the psychophysical processes in the sensing subject was the study of the action currents of the human retina.

Cooper, Creed, and Granit [9] recorded the retinal action potential of the human eye with a string galvanometer and a direct-coupled amplifier under standard conditions. They found that the responses from the periphery of the retina (30 degrees from the fixation point) resembled those from the center in general features, but that less potential was developed in the periphery. Their b-wave was about 0.2 millivolt (mv). With intermittent illumination at slow rates of alternation the responses showed corresponding ripples in the electric record.

Gröppel, Haass, Kohlrausch,[10] in 1938, used a nonpolarizable zinc electrode, consisting of a short glass tube which contained an amalgamated zinc rod in concentrated watery solution of zinc sulfate. The part near the eye was filled with Ringer's gelatin, in which a small cotton wick was placed. The indifferent electrode consisted of a glass funnel, which was placed on the temple. This also contained a zinc electrode in Ringer's gelatin. The currents were magnified 50 times by a direct-coupled amplifier and were photographically registered by a string galvanometer with a magnification of about 700.

Bernhard,[6c] in a paper published in 1940, reported the study of the electroretinogram and its relation to the alpha-blocking time and the motor reaction time. He used a direct-coupled amplifier and an oscillograph.

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7. Karpe, G.: Apparatus and Method for Clinical Recording of the Electroretinogram, Docum. ophth. **2**:268-276, 1948.

8. Sachs, E.: Die Aktionsströme des menschlichen Auges: Ihre Beziehung zu Reiz und Empfindung, Klin. Wchnschr. **8**:136-137, 1929.

9. Cooper, S.; Creed, R. S., and Granit, R.: Note on the Retinal Action Potential of the Human Eye, J. Physiol. **79**:185-190, 1933.

10. Gröppel, F.; Haass, F., and Kohlrausch, A.: Aktionsströme und Gesichtsempfindungen des menschlichen Auges, Ztschr. Sinnesphysiol. **67**:207-226, 1938.

Adrian,[11] in 1944, 1945, and 1946, published three papers on the electric response of the eye, with special reference to scotopic and photopic activity.

The contact lens was introduced by Riggs [12] in 1941 and Karpe [3] in 1945. Most of the clinical electroretinographic studies are done with one of these lenses.

PHYSIOLOGIC BASIS OF THE ELECTRORETINOGRAM

The work of von Brücke and Garten (1907) and Piper (1911) has made it clear that the main features of the vertebrate electroretinogram are as follows: an initial negative a-wave, a positive b-wave, a slow secondary c-wave, and an off-effect, or d-wave (Fig. 1). Their relative importance in making up the electroretinogram may vary much.[1] It will be noticed that the a-wave lasts but a very short time, less than 0.1 second. It is followed immediately by the strong positive b-wave. This also falls away and is replaced by a further rise in the positivity, the c-wave, which lasts until the light is turned off. At this point a new deflection, the d-wave, appears.[13]

There are two types of retinas, the E-retina and the I-retina. The E-retina is characteristic of all mammals, including man. The chief difference between the two

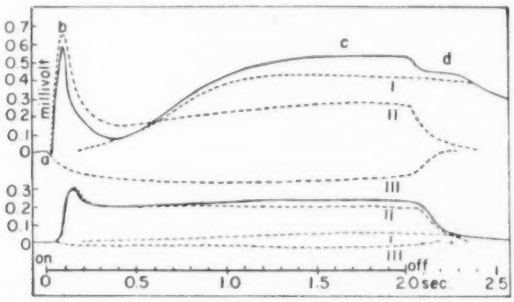

Fig. 1.—Analysis of the E-electroretinogram at two intensities: upper, 14 mv; lower, 0.14 mv. The a-wave has been broadened slightly out of proportion to demonstrate its derivation more clearly (Granit [1]).

types is the much larger off-effect found in the latter. Usually the I-retina also has a larger a-wave, and this distinction becomes more marked after light adaptation. Another difference is the response to flicker frequency. The E-retina is characterized by a rather low fusion frequency in the photopic state, and it also responds to flicker primarily with volleys of excitation. The I-retina responds with a series of negative waves[13a,b] (Fig. 2).

Three components are thought to constitute the electroretinogram; they are designated as P I, P II, and P III (Figs. 1 and 2).

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11. Adrian, E. D.: Rod and Cone Responses in the Human Eye, Nature, London **154**:361-362, 1944; Electric Response of the Human Eye, J. Physiol. **104**:84-104, 1945; Rod and Cone Components in the Electric Response of the Eye, ibid. **105**:24-37, 1946.

12. Riggs, L. A.: Continuous and Reproducible Records of the Electrical Activity of the Human Retina, Proc. Soc. Exper. Biol. & Med. **48**:204-207, 1941.

13. (*a*) Granit,[1] (*b*) Adler, F. H.: Physiology of the Eye: Clinical Application, St. Louis, C. V. Mosby Company, 1950. (*c*) Spielberg, P. I.: Problems of Physiological Optics (Action Currents of Human Eye), Acad. Sc. U. S. S. R. **2**:127-135, 1944.

P I is recorded as the c-wave of the electroretinogram. This retinal c-wave has to be differentiated from the pupillary response that simulates a c-wave, which is obtained when the corneal electrodes are near the limbus or on the cornea, but cannot be obtained on the sclera.[14] This wave disappears if the pupil is immobilized.[3]

The retinal secondary c-wave can be obtained from any part of the globe. Wirth [15] isolated a slow potential change in man with an intensity of 8 lux and a visual angle of 8 degrees, which occurred after a latency of 0.3 second. This reached a maximum of 0.18 mv and returned to the base line without any off-effect. In animals the latent period of the c-wave, or P I, varies from about 0.5 second, in the cat, to from 2 to 6 seconds, in the frog. The potential may reach a maximum of 2.0 mv in the frog and of about 1.0 mv in the cat.[13a,b]

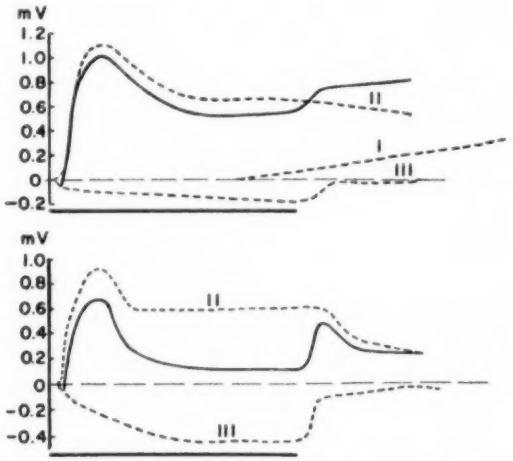

Fig. 2.—Analysis of the components of the frog's retinal action potential (drawn in full) in dark adaptation (upper set of curves) and light adaptation (lower set of curves). Components are drawn in broken lines. The thick black line indicates a stimulus of two seconds' duration (Granit, R., and Riddell, L. A.: J. Physiol. **81**:1-28, 1934).

The c-wave is always absent with short stimuli and can be isolated only when a prolonged stimulus of moderate intensity is used. With rhythmic illumination it is present only after the first stimulus.[14] It is seen only after adequate dark adaptation and is diminished or disappears on light adaptation both in the E-retina of the cat and in the I-retina of the frog. However, under the action of epinephrine the c-wave can be demonstrated after light adaptation in the frog's eye. It is the first to disappear from the electroretinogram of the cat under ether anesthesia. The c-wave is absent from the electroretinogram if the stimulating light is of suffi-

14. Dodt, E.: Beiträge zur Elektrophysiologie des Auges: Über die sekundäre Erhebung im Aktionspotential des menschlichen Auges bei Belichtung, von Graefes Arch. Ophth. **151**: 672-692, 1951.

15. Wirth, A.: Caratteri dell'elettroretinogramma nell'uomo, Ann. ottal. e. clin. ocul. **76**: 109-123, 1950; Beiträge zu den Teilströmen des menschlichen Elektroretinogramms, von Graefes Arch. Ophth. **151**:662-671, 1951.

ciently long wave length not to stimulate the rods.[13a,b] Granit and Wrede noted that it is possible to decide on the basis of P I when the activity of the rods begins in the very first stage of dark adaptation.[1]

Wirth [15] assumed that P I is the expression of that initial mechanism which is due to the excitation of the rods. The fact that P I disappears even in transient light adaptation would indicate that this phase represents a transitional period and expresses what takes place in the transition from scotopic to the photopic state. When the stimulus is increased in length and intensity, a transient state of light adaptation occurs, and this explains the reduction and disappearance of the c-wave. When a rather strong stimulus produces a b-wave, a period of insensitivity of certain duration follows. This corresponds to the fact that one is blinded when one goes from dark to light. Granit [16] suggested, therefore, that P I to some extent offsets this insensitivity of the visual apparatus and permits the eye to adapt to newer conditions more readily. It has the ability to sensitize P II, and this must be of great visual importance at the moment of transition from dark to light adaptation.

Dodt [14] considered the retinal c-wave as the electromotor equivalent of the migration of pigment and movement of the cones with changing adaptation. He based this conclusion on an old finding by Grijns, who noted that illumination of the dark-adapted frog eye led to a difference in potential in the other eye, even though it was not illuminated. Also, the c-wave is higher in the frog than in man, and this difference may be due to less movement of pigment in man than in the frog.

P II forms the b-wave, which is the best electrophysiologic expression for the sensitivity of the retina. It is used as a measure of the retinal effects when one is investigating the sensitivity of the retina in different states of adaptation, its relation to different wave lengths equalized with respect to energy, and its relation to the concentration of visual purple in varying conditions.[1]

Many observers have noticed that in the electroretinogram of the dark-adapted eye the b-wave shows a "staircase" effect, the later responses being enhanced as a result of the first few stimuli. Since it is the b-wave that is affected, one must infer that P II is involved.[1]

Others have noticed small additional oscillations on the b-wave, due to synchronous discharge of various retinal elements.[17] Granit [1] suggested that the retinal elements which respond to light with the reaction P II do not all behave alike. The P II component of the electroretinogram therefore represents the sum total of a number of processes with different latent periods and rates of appearance, which produce different amounts of positive potential.

P II is the only component that is associated with impulse response in the optic nerve, and by eliminating P II the impulse discharge in the nerve disappears.[16] Anything which affects the optic nerve discharge will affect P II in the same way; an augmentation of the discharge is generally associated with an increase of P II, and vice versa. A slow late b-wave on the electroretinogram also corresponds to a slowly rising and delayed discharge in the nerve. However, since the b-wave is the average result of the activity of many P II processes, this correspondence holds only for the over-all reaction, and is not necessarily true for the responses of single

16. Granit [1]: Isolation of Components in the Retinal Action Potential of the Decerebrate Dark-Adapted Cat, J. Physiol. **76**:1P-2P, 1932.

17. Wirth, A.: Alcune osservazioni cliniche di elettroretinografia, Atti Soc. oftal. ital. **12**: 199-209, 1951.

fibers. The size of the P II response roughly reproduces something which one might call the intensity, or quantity, of the effect which is carried to the brain as a sensory message.[13a,b]

Therman has found that strychnine enhances both the b-wave and the off-effect, regardless of the stimulating wave length used. This general excitatory effect is followed by a depression of P II activity. Physostigmine and acetylcholine have a depressing effect, although with physostigmine this is occasionally preceded by a transient excitation. Atropine greatly increases the size of the b-wave when short wave lengths are used as stimuli, but it never has much effect on the d-wave. Both these findings suggest that atropine excites the rods, but not the cones. Nicotine has a very small, uncertain, and transiently exciting effect on P II, but it tends to stimulate a spontaneous optic nerve discharge, as well as to increase the synchronization of its responses to light. With ether inhalation, P II is removed after P I.[1]

P II is highly sensitive to the oxygen supply. Interference with respiration or circulation, as by compression of the carotid arteries, may lead to a selective removal of P II, leaving an electroretinogram representing the sum of the effect of P I and P III.[1] In rabbits Noell and Chinn [18] found during anoxia that the a-wave of the electroretinogram generally diminished in amplitude during the late decline of the b-wave, so that only a small a-wave was present after the b-wave had disappeared. Noell,[19] in a more recent report, found that in rabbits the a-wave declined faster than, or at least as fast as, the b-wave. In the cat and monkey the b-wave disappeared before there was any measurable reduction in the size of the a-wave. In man the b-wave had only moderately decreased at the time that sensation was lost.

According to Granit,[1] P II is localized to the synaptic layers of the retina. Bartley,[20] in 1939, suggested that P II might be localized in the bipolar cells, and Granit [1] found this view very probable. P II is thus an indication that the wave of excitation has activated the synaptic layers of the retina.[21]

P III is thought to be responsible for the initial a-wave. It has several properties in common with the pure receptor potentials of vertebrate eyes, but it is of the opposite electrical sign and has been shown to precede P II.[21a-c] It is the last to disappear when the subject is under ether anesthesia, and, like P I, it is small at low intensities of light.[13b] The negative P III in the frog eye, isolated by means of potassium, agrees with the first phase of the a-wave and the off-effect in the normal electroretinogram as regards its initial fall and return to the base line in time relation and rate of rise.[6c] It is believed that P III is more prominent in eyes dominated by cones, whether it be one with a pure-cone retina or one with a mixed retina which is light-adapted.[1]

The a-wave is noted in the light-adapted state and point-like stimulation of the macula. When the light stimulus is concentrated in the macular area in the light-adapted state, a sufficient number of cones enters into action to produce a manifest electric action. Such a reaction is quite evident in the first electroretinogram and

18. Noell, W., and Chinn, H.: Failure of the Visual Pathway During Anoxia, Am. J. Physiol. **161**:573-590, 1950.

19. Noell, W.: Site of Asphyxial Block in Mammalian Retinae, J. Appl. Physiol. **3**:489-500, 1951.

20. Bartley, S. H.: Vision: A Study of Its Basis, with a Historical Perspective by Edwin G. Boring, New York, D. Van Nostrand Company, Inc., 1941.

21. (*a*) Granit.[1] (*b*) Karpe.[3] (*c*) Adler.[13b] (*d*) Bartley.[20]

decreases in successive ones. This might be due to a relationship between P III and alpha adaptation.[15] An a-wave is nearly always present with a stroboscopic light of intensity greater than 500 lux.[22]

The belief that P III is connected with inhibition has been confirmed by the alcohol test, which cuts down the activity of P III selectively and always results in decreased inhibition. The a-wave and inhibition precede the excitatory effect of light in the I-retina, and at higher intensities in the E-retina. This would be advantageous to an animal being constantly stimulated if the preceding stimulus were cleared before a new stimulus was applied.[13b] In summary, the negative process P III preceded the P II component and is somehow connected with inhibition. It is probable that it also initiates P II, and thereby initiates excitation in the retinal structures distal to those in which its own generation leads to inhibition.[1]

The d-wave, or "off-effect," is believed to be the result of interference between the positive potentials developed in the b- and c-waves with the negative a-wave rebound. If the latter has been an especially large negative potential, the rebound may produce a positive deflection, or d-wave, which is carried into the optic nerve fibers as a burst of impulses at off.[13b]

Figure 2 shows the difference in the frog electroretinogram in dark and in light adaptation. The amplitude of the b-wave diminishes with increasing light adaptation, the electroretinogram falling toward the base line, and the off-effect shows a more rapid increase to higher amplitude. When P II is partially or totally eliminated, the off-effect can take place entirely on the negative side. The light-adapted state is consequently characterized by the absence of the P I component and a striking change in the P III process, which increases in size and shows increased rapidity when returning to the base line at the same time that the off-effect increases in amplitude. This change of P III can take place without a simultaneous change in P II.[9c]

There is still confusion as to how the various parts of the electroretinogram are related to the activity of rods or cones. Karpe and Tansley [23] and Tansley [24] believed that the evidence is clear that the negative potentials are predominately associated with cones. An increase in cone activity, as in light adaptation, produces an increase in the negative potentials. Where cone responses are negligible, as in dark adaptation, it is doubtful whether any significant negative potential is developed. P II, or the b-wave, cannot in general be so closely linked with the rods. In fact, it is evident that the b-wave can be the result of either rod or cone activity, as it can be evoked by stimulating any normal retina (even a pure cone one) with an adequate stimulus.

METHODS OF INVESTIGATION

Briefly, the apparatus consists of two electrodes, one connected to the cornea, or near the cornea, and a reference electrode, an optical system for stimulating the eye, an amplifier, and a photographic recording device.

Electrodes.—Two types of corneal electrodes are now in use; the contact glass, described by Karpe [3] or Riggs,[12] and the d'Arsonval type, or cotton-wick electrode, used by Adrian.[11]

22. Euzière, J.; Passouant, P., and Cazaban, R.: Temps objectifs de fusion et excitations lumineuses doublées en électro-rétinographie, Ann. ocul. **184**:865-876, 1951.

23. Karpe, G., and Tansley, K.: Relationship Between the Change in the Electroretinogram and the Subjective Dark-Adaptation Curve, J. Physiol. **107**:272-279, 1948.

24. Tansley, K.: Physiological Basis of Electroretinography, Proc. 16th Internat. Congress Ophth., London **2**:583-590, 1950.

Riggs [12] uses a corneal electrode mounted on a contact lens. The electrode consists of a silver disc cemented into a hole in the contact lens. A fine, flexible wire supported by beeswax is employed as a lead from the electrode. When the lens is inserted into the eye, the silver makes contact with the isotonic sodium chloride solution, between it and the cornea. A neutral electrode, consisting of a cup filled with saline solution, is applied to the skin of the subject over the cheekbone. The stability of these electrodes is such that records may be taken over a period of an hour or more, with satisfactory reproducibility.

Karpe's [3] active electrode consists of a chlorinated silver rod screwed into a bottle neck in a plastic contact glass. The glass is filled with isotonic sodium chloride solution. In addition, there are two other electrodes: one an indifferent one, which is a chlorinated silver plate fixed to the inside of a plastic headband and applied to the patient's forehead. This headband also carries all leads from the patient to the amplifier. The third electrode used by Karpe connects the metal spring speculum to the metal shielding of the apparatus. Karpe believed that this connection is important, as it provides adequate neutralization of active interference, which usually permits the electroretinogram to be taken in an ordinary room without electric shielding. A similar electrode was used by Asher.[25]

Monnier and associates,[26]; Spielberg [13c]; Wirth,[17] and Euzière, Passouant, and Cazaban [22] use essentially the same electrode as Adrian,[11] although the technique of the various authors differs in some details. Adrian's electrode consists of a moist thread making contact with the exposed part of the eyeball on the nasal side of the cornea. The thread protrudes 2 to 3 mm. from a narrow glass tube filled with saline solution and fixed with plasticene® between the bridge and the rim of a pair of spectacles. One end of a fine silver wire is coiled around the thread near its exit from the tube, and the other end connects with an insulated lead fastened to the side-member of the spectacle frame. The coil of silver wire in the tube is coated electrolytically with silver chloride. The electrode is fixed so that when the spectacle frame is in its proper place the moist thread touches the conjunctiva somewhere between the margin of the cornea and the inner canthus of the eye.

The cotton-wick electrode was used initially by Karpe [3] but was abandoned. He observed that shifting of the point of contact with the sclera influenced the results. The leads apparently were very sensitive to local potential changes of extraretinal character. The fine tip of the cotton wick, moreover, required a steady fixation which few patients could maintain. A further difficulty arose from blinking sweeping the electrode away. When the eyelids were held apart with a spring speculum to avoid blinking, it was necessary to drop saline onto the globe to prevent corneal erosion. Wirth [17] found that the b-potential was about one-third less when measured with the cotton-wick electrode than when measured with the contact lens.

In order to avoid difficulties arising from the use of a contact lens or other electrodes placed directly on the cornea, Motokawa and Mita [4] devised an electrode consisting of tin foil, which was placed on the root of the nose and temple on the side of the eye to be examined. By means of this arrangement, the authors were able to obtain satisfactory electroretinograms, although they admit that with this method the disturbances due to electroencephalographic potentials in the record were more prevalent than with the corneal electrodes.

Electric and Recording Technique.—Karpe [3] at first used a direct-coupled amplifier which was connected to an oscillograph set up with a camera and time marker. Later he used a condenser-coupled amplifier with a time constant of approximately 1.5 seconds. The records were made on a moving photographic film by means of two oscillographs, one for the actual electroretinogram and the other for the stimulus which was connected to the photoelectric cell in the stimulus lamp.[7]

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25. Asher, H.: Human Electro-Retinogram, J. Physiol. **113**:34P, 1951.

26. Monnier, M., and Boehm, F.: Technik der Elektroretinographie beim Menschen, Helvet. physiol. et pharmacol. acta **3**:C25-C27, 1945; Objektivierung der Lichtrezeption in der Netzhaut durch das Elektroretinogram beim Menschen, ibid. **3**:C39-C41, 1945. Monnier, M., and Amsler, M.: Examen objectif de la fonction rétinienne par l'électro-rétinogramme dans un cas de rétrécissement concentrique du champ visuel, Ophthalmologica **110**:225-241, 1945. Monnier, M.: L'état actuel de nos investigations électro-rétinographiques chez l'homme, Confinia neurol. **8**:357-359, 1947-1948.

Riggs and Johnson [27] used a high-gain, direct-coupled amplifier. The output of this amplifier was used to actuate the first element of the recording device, an oscillograph. A beam from the mirror of the oscillograph made a trace upon a moving strip of photographic paper. The resulting records showed the exact magnitude and wave form of the retinal action potentials built up on response to flashes of light.

Monnier [28] amplified the potential about 2,000,000 times with a three-stage, push-pull amplifier and direct coupling. Again, registration was with the oscillograph.

Wirth [15] used a capacity-coupled amplifier with an adequate time constant to register slow phenomena. A cathode-ray oscillograph with photographic recording device was used.

Euzière, Passouant, and Cazaban [22] used a six-channel electroencephalographic ink writer to record simultaneously the electroretinograms and the electroencephalograms.

The electroretinogram is usually recorded with the patient in a supine position. At first it was thought necessary to record the electroretinogram in an electrically shielded room, but this precaution has been abandoned.[3]

Illuminating Technique.—Karpe [7] used as a stimulus light the amount provided by a 25-watt bulb. This is connected to a relay, which lighted it for about 1/7 second, the required intensity being maintained for about one-third of this time. At a distance of 140 cm. this lamp gave a standard illumination of about 20 lux at the eye. This was varied by moving the lamp nearer or farther from the patient. The onset and cessation of the stimulus were recorded by means of a photoelectric cell placed near the bulb inside the shade of the lamp. The filament was constantly fed by a weak current, so that it glowed faintly and thus served as a fixation point.

Riggs and Johnson [27] used a flash of light of 0.04 second and 7 degrees 30 minutes in diameter. A red fixation point assured central fixation.

Monnier and associates [29] used a 6-volt, 15-watt lamp. The beam was concentrated by means of lenses and diaphragms, and the lamp itself remained on, so that its time constant played no role. The duration of the illuminating phase was determined by a shutter, controlled by a small electromagnetic relay. A flicker stimulation was obtained in this way. Optimum electroretinograms were obtained with flicker frequencies so arranged that an illumination of 0.1 second was followed by a dark period of 0.9 second. Isolated prolonged stimuli of 2 seconds followed by a dark period of 3 minutes also produced excellent electroretinograms. Five levels of illumination were employed, the second being 0.1 lumen at the retina.

Monnier and colleagues [29] studied the electroretinogram with particular reference to the perimetric electroretinogram. The patient was seated in front of a perimeter, in the arc of which an apparatus was marked for the stimulation of light. There was a movable arrangement, consisting of a light source, aperture, lenses, and color filters. This permitted one to project on the various parts of the retina a circumscribed spot of definite wave length and controlled duration and intensity. Tests on pig eyes have shown that the size of the spot is somewhat below 2 degrees. The human eye to be examined was centered in front of the perimeter, fixating a small red light in the center of the arc.

Salleras [30] used a 50-watt lamp mounted in a photographic camera with an aperture which could be regulated by electromagnetic relay. The duration was 0.04 second, and this produced an intensity of 20 lux at 10 degrees on the retina.

Wirth [15] used batteries to produce a light of 6 to 7 lux, either white or red. The lamp had a voltage of 8, with a condensing lens and light shutter manually controlled to maintain a stimulus of 0.04, 0.02, or 0.01 second in duration. In front of the light were apertures which gave a visual angle at 30 cm. of 8, 4, or 2 degrees, depending on the aperture used.

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27. Riggs, L., and Johnson, E.: Electrical Responses of the Human Retina, J. Exper. Psychol. **39**:415-424, 1949.

28. Monnier, M.: L'électro-rétinogramme de l'homme, Electroencephalog. & Clin. Neurophysiol. **1**:87-108, 1949.

29. (*a*) Monnier.[28] (*b*) Monnier, M., and Boehm, F.: Beiträge zum Elektroretinogramm des Menschen: I. Perimetrische Elektroretinographie, Helvet. physiol. et pharmacol. acta **5**:205-224, 1947.

30. Salleras, A.: Electrorretinografía clínica (nuestras observaciones), Arch. oftal. Buenos Aires **25**:1-12, 1950.

Euzière and associates [22] used an ordinary stroboscopic light at 33 cm. from the eye. The duration of the stimulus was 10 milliseconds, with an intensity higher than 500 lux.

Technique of Adaptation.—Karpe [31] initially registered the electroretinograms in both light and dark adaptation. For light adaptation, the standardized illumination was about 5 lux at the eye. The patient remained in this illumination for 15 to 20 minutes. A standardized state of dark adaptation was obtained by keeping the patient in complete darkness or in an illumination of not more than 0.1 lux for five minutes after standard light adaptation.

Wirth [15] used a standard illumination of 6 to 7 lux for light adaptation and allowed the patient to remain at this illumination for 15 to 20 minutes. For semi-dark-adaptation a light of 0.1 to 0.05 lux was used for five to seven minutes.

Sources of Error.—With the cotton-wick type of electrode, there is an increase in the negative after-swing if the electrode is placed outside the limbus. Mydriatics remove this negative after-effect, which is thought to be due to the negativity of the iris muscles.[3]

The contact glass, if improperly placed, will also give some variation in the b-potential. Karpe [3] believed that this is the main methodical error in the evaluation of a representative b-wave of a series. Large bubbles under the glass interrupted the contact between the cornea

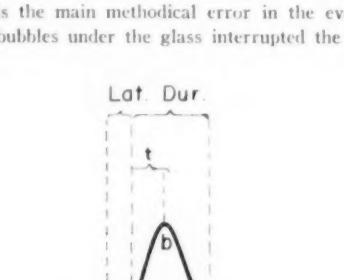

Fig. 3.—Diagram of scotopic human electroretinogram in response to flash S. The a- and b-waves are marked by corresponding letters. *Lat.* indicates latency; *Dur.*, duration of b-wave; *t*, culmination time. Alternatives for changes in succeeding b-waves are marked in the figure. Adapted from Karpe,[3] p. 56.

and the electrode. Small bubbles did not prevent recording, but if the patient could not avoid blinking after stimulation the b-wave often tailed off into a negative swing.

Blinking can produce an elevation similar to the b-wave. However, this usually has a longer latency period, and when the blink wave is added to the top of the b-wave it is generally possible to discover the extraretinal potential by analysis of a series of records.[3] With reduced intensity and time, Wirth [17] believed that blinks are not very important.

Rotation of the globe behind the contact glass leads to a shift of the base line, which makes interpretation of the electroretinogram more difficult.[3] If the patient has good fixation, these will be eliminated for the most part.[17]

THE NORMAL HUMAN ELECTRORETINOGRAM

With a stimulus of short duration, the electroretinogram consists of an a- and a b-wave (Fig. 3). Late secondary rises due to component P I, as well as the off-effect, can be avoided with brief flashes.[32]

Karpe [3] recorded a number of electroretinograms in the light-adapted state and found that with his technique the electroretinogram was too small to measure in

31. Karpe, footnotes 3 and 7.

32. Karpe,[3] Tansley.[24]

some cases. It was merely possible to state whether the a-wave was present or absent. The mean for the b-wave potential was 0.07 mv, and the duration was 0.10 second. The average latent period for the b-wave was 0.03 second.

Wirth [15] with a stimulus of 8-degree size, 20-lux intensity, and a duration of 0.04 second, found a small b-wave, and at times a small a-wave, in the light-adapted state. If a point-like stimulus was used, so that presumably the macula was stimulated, only a negative deviation was noted, which was present in the first electroretinogram and immediately decreased, especially if the stimulus was repeated at short intervals.

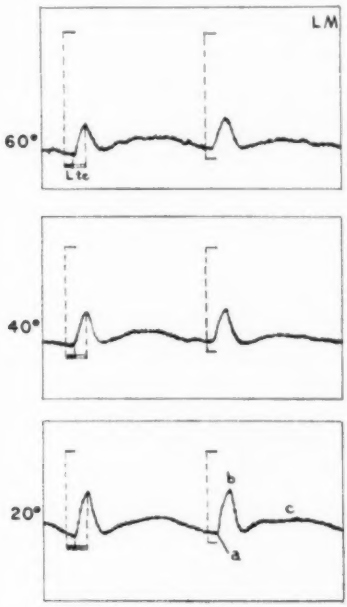

Fig. 4.—Influence of stimulated area of retina on electroretinogram (nasal field). Amplitude of the b-potential increases when the luminous spot is moved from 60 to 20 degrees, excentrically. *L* indicates latent period of b-potential; *t. c.*, culmination time; *a*, initial potential, which becomes more pronounced as luminous spot approaches the center. Adapted from Monnier,[28] p. 97.

The scotopic electroretinogram is much larger than the photopic one, which decreases the relative magnitude of error in measuring the potentials. Karpe [32] found that the a-wave was lacking in most scotopic electroretinograms. The b-wave varied between 0.23 and 0.51 mv, with a mean value of 0.35 mv. The mean value of the duration of the b-wave was 0.15 second, while the mean value of the latent period was 0.04 second. Jacobson and O'Brien [33] reported an average value of 0.28 mv. Wirth [17] and Monnier and Boehm [29b] found with the cotton-wick electrode that the b-wave potential varied from 0.16 to 0.33 mv.

33. Jacobson, J. H., and O'Brien, J. M.: First Results of Clinical Electro-Retinography, personal communication to the author.

Monnier [28] found that in normal persons the typical b-wave potential began after a latent period of 0.05 to 0.08 second and reached its maximum after 0.05 to 0.10 second. The amplitude of the b-wave potential was increased on stimulation of the more central area of the retina. This is shown in Figure 4 and Table 1. At the same time the culmination time decreases on stimulation of the more central areas (35% shorter at 20 degrees than at 60 degrees).

Euzière and associates,[22] using the stroboscopic light, found that the a-wave was always present. The amplitude varied from 0.050 to 0.80 mv, with a duration of 0.032 to 0.048 second. Its latent period varied from 0.013 to 0.016 second. The b-wave potential varied from 0.090 to 0.150 mv, with an average of 0.110 mv. The duration was 0.112 to 0.160 second, with an average of 0.148 second. Regardless of the duration of the b-wave, the culmination time was always found to be about 0.08 second, so that variations in the duration of the b-wave were thought to be due to the descending phase of the b-wave.

With a stimulus of 8 lux and a visual angle of 8 degrees, Wirth [15] was able to register a slow potential change, which occurred after a latency of 0.3 second and corresponded to the c-wave. This wave slowly increased, reached a maximum of

TABLE 1.—*Decrease in b-Potential (Microvolts) as Distance from Macula Increases**

	White Light			Green Light			No. of	
Area of Field	60°	40°	20°	60°	40°	20°	ERG's	Subject
Temporal	99	135	172	80	62	96	169	H. M.
	139	177	178	62	88	88	145	L. M.
Inferior	...	231	265	...	141	172	84	H. M.

* Adapted from Monnier, M.: L'électrorétinogramme (ERG) chez l'homme et le contrôle objectif du champ visuel par la périmétrie L'électrorétinographique, Compt. rend. Soc. biol **140**:231, 1946.

0.18 mv, and returned to the base line without any off-effect. The a- and b- waves were not seen. By slowly increasing the strength of the light, a b-wave appeared, of varying amplitude, while the c-wave remained unchanged. With a further increase, the b-wave became very pronounced, and the c-wave became faster and less obvious. At 40 lux, no a- and c-waves were found.

EFFECT OF INTENSITY ON RETINAL RESPONSE

The relationship of the intensity to the retinal response has been studied in both man and animals. For low intensities, the amplitude of the b-potential is proportional to the fourth root of the stimulus.[15] For higher intensities, the b-potential is approximately proportional to the log stimulus intensity, whereas the latent period shortens.[34] In the normal dark-adapted eye the height of the b-wave increases with increasing stimulus intensity, until a maximum is reached at 20 lux. This curve begins to flatten out at about 5 lux. Further increase in intensity tends slightly to decrease the height of the b-wave, as seen in Figure 5.

34. (*a*) Karpe.[3] (*b*) Motokawa and Mita.[4] (*c*) Wirth.[15] (*d*) Karpe and Tansley.[23] (*e*) Tansley.[24]

This is also illustrated by Table 2, from Motokawa.[35]

It will be noted that the intensity, in lux reached a higher level in these data before there was a drop in the b-potential. This may be due to the variation in technique.

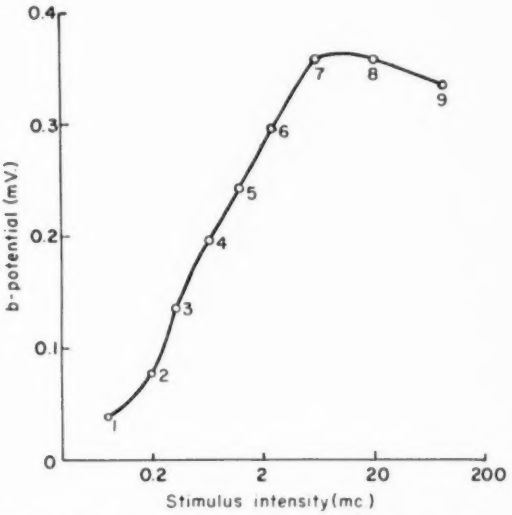

Fig. 5.—Effect of stimulus strength on size of b-wave of dark-adapted eye. The first electroretinogram was recorded after complete dark-adaptation for 40 minutes; the intensity of the stimulus was changed by means of neutral-tint filters; no stimulus was applied until the eye had recovered its dark-adapted subjective sensitivity. On the abscissae are plotted the log stimulus intensity, on the ordinates, the b-potential, in millivolts. Adapted from Tansley,[24] p. 586.

TABLE 2.—*Variation of b-Potential, in Millivolts, with Change in Intensity of Stimulating Light**

Intensity, Lux	b-Potential, Mv
0.34	0.015
1.12	0.020
2.24	0.022
13.4	0.035
67.0	0.041
559.0	0.033
1,676.0	0.026

* Average of two experiments.

EFFECT OF ADAPTATION AND COLOR

Adrian [11] believed that the electric response of the human eye to a flash of light could be divided into a rapid and a slow component; the former was present in the light-adapted eye and was more prominent with light of longer wave length (red) and the latter was more prominent after dark adaptation and with light of shorter

35. Motokawa, K.: Das Elektroretinogramm des Menschen und seine Beziehung zur Unterschiedsschwelle der Lichtempfindlichkeit und zur Sehschärfe, Jap. J. M. Sc. **8**:135-147, 1942.

wave lengths. With red light, the response of the electroretinogram is a brief diphasic change, the cornea becoming initially negative. This response is very little affected by dark adaptation, though there is some increase in the first few minutes. Riggs, Berry, and Wayner [36] found in the dark-adapted eye on stimulation with red light a brief diphasic component of the b-wave. Adrian [11] concluded that the first peak of the double-peaked b-wave was photopic in origin, while the second peak, which was ordinarily the dominant one, was scotopic. Only red light favors the photopic system sufficiently to allow the small photopic component to escape domination by the scotopic component. Riggs and Johnson [27] found that this brief diphasic component may appear in reduced amount in responses to light of intermediate wave lengths.

The response of the eye to blue light is a slower monophasic change without a long latency. This response is greatly affected by dark adaptation and may be too small to detect in the first few minutes after the eye has been exposed to a bright sky.

Riggs, Berry, and Wayner [36] found that the electrical data on the spectral sensitivity of the dark-adapted eye seem to parallel the scotopic matching data for all

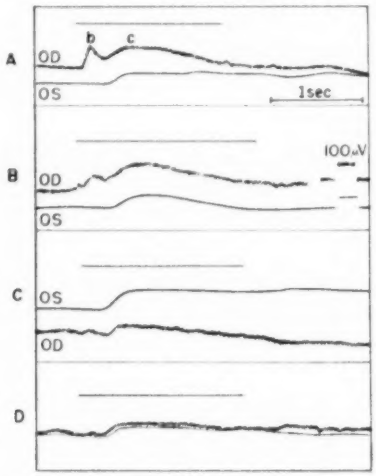

Fig. 6.—Binocular retinography in man. Response to illumination in the right eye with a light ray forming an angle of 60 degrees with the fixating light. *A*, white; *B*, blue; *C*, green; *D*, red. Time is expressed in seconds, and amplitude, in microvolts. Primary elevation is indicated by *b*; secondary elevation by *c*. Adapted from Monnier,[37] p. 2.

except the blue region of the spectrum. They found, also, that the electric response of the light-adapted eye fails to reveal any shift from a scotopic to photopic spectral sensitivity curve. They believe this is additional evidence to support the conclusion that the b-wave of the human retinal response is scotopic in origin.

Karpe and Tansley [34d,e] found that the b-potential curve showed a good agreement with the rod part of the subjective dark-adaptative curve if the electroretinographic stimulus was of moderate strength and the experiment was preceded by an efficient light adaptation. There was also good agreement without the preceding light adaptation if the electroretinographic stimulus was strong enough.

36. Riggs, L. A.; Berry, R. N., and Wayner, M.: Comparison of Electrical and Psychophysical Determinations of the Spectral Sensitivity of the Human Eye, J. Optic. Soc. America **39**:427-436, 1949.

Monnier and Boehm [29b] found that the scotopic component is particularly pronounced when the peripheral areas of the retina are stimulated.

Monnier [37] and Dodt [14] have also recorded binocular electroretinograms in man. A normal electroretinogram is produced at the stimulated, ipsilateral eye, and a bioelectric consensual response is produced at the contralateral eye. The latter response consists in a positive deflection, corresponding to increased electropositivity under the corneal electrode. A close relationship exists between the consensual response and the secondary rise (c-potential) of the ipsilateral electroretinogram. Monnier originally believed that this consensual response could be identified with the c-potential. Jacobson and Berens [38] were of the opinion that this response probably resulted from recording the action potentials of the sphincter pupillae. Figure 6 shows the binocular response to different colors.

FLICKER FUSION FREQUENCIES

Spielberg,[13c] Euzière and associates,[22] and Babel and Monnier [39] have studied the flicker fusion frequencies. If the eye is stimulated by intermittent light, a kind of ripple is observed on the electroretinogram, which repeats the rhythm of flickering stimuli. This ripple will not disappear until a certain flicker frequency is attained by the light. After the flicker frequency has surpassed the limit, a smooth line is recorded on the electroretinogram in spite of the fact that the light stimulus is still sent intermittently.

Babel and Monnier [39] found that with 18-stimuli per second flicker was still present. With 20 to 22 stimuli per second it became difficult to distinguish the individual responses in the electroretinogram. With 23 stimuli per second the fusion threshold was attained in old subjects. The authors also found that the fusion frequency was higher when they were stimulating the central region (20 to 23 stimuli per second) than when stimulating the periphery (16 to 17 stimuli per second at 60 degrees temporally). The objective threshold of the flicker fusion frequency is equal to, or even slightly below, the subjective threshold.

Euzière and associates [22] found on increasing the frequency of stimuli to 4 to 6 per second that there was almost complete disappearance of the b-wave. At a frequency of 13 stimuli per second, a tracing of special morphology, the biplex rhythm, was noted. This persisted until a sinusoidal rhythm appeared, between 23 and 28 stimuli per second, and its amplitude decreased as the frequency increased. The tracing became completely flat at about 52 stimuli per second, with a variation of 48 to 56 stimuli per second. The subjective fusion time with the same instrument corresponded to 52 cps. These figures were much higher than those of Monnier; however, it had been found by other authors that flicker fusion frequency increased with very short and very intense stimuli. This fact was attributed to the very great amplitude of the P III component under these conditions of stimulation.

37. Monnier, M.: Les manifestations électriques consensuelles de l'activité rétinienne chez l'homme (électrorétinographie binoculaire), Experientia **2**:1-5, 1946.

38. Jacobson, J., and Berens, C.: Clinical Electroretinography: A Review of the Literature, Quart. Rev. Ophth. **7**:99-107, 1951.

39. Babel, J., and Monnier, M.: Détermination objective de la fréquence de fusion par l'électro-rétinographie chez l'homme, Helvet. physiol. et pharmacol. acta **7**:(Pt. 2) C3, 1949.

RELATION OF THE ELECTRORETINOGRAM TO CORTICAL RESPONSES

This relation has been studied by Monnier and associates,[40] Bernhard,[6c] Euzière and associates,[22] and Spielberg.[41]

Among the cortical rhythmic potentials, the dominating one is the "alpha rhythm" of about 10 waves per second, described by Berger. Bernhard[6c] found a striking blocking of the alpha rhythm after a light stimulus under appropriate conditions. The blocking usually takes place with a sudden interruption in the regular rhythm; however, the last alpha waves sometimes show diminished amplitude before the blocking. This fact sometimes makes it difficult to form an exact judgment of the blocking time.

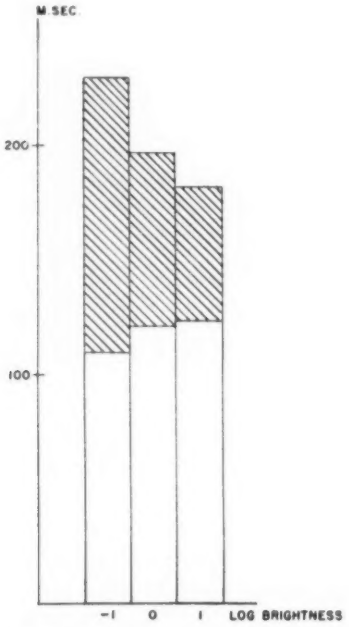

Fig. 7.—Diagram showing relation between blocking time (whole column, both shaded and unshaded part) and latency of the retinogram (shaded part) at light intensities of 1, 0.1, and 0.01. Time is expressed in milliseconds. (Bernhard,[6c] p. 76.).

The alpha blocking does not appear until the b-wave maximum of the electroretinogram has passed, indicating that a "central period," from the "hidden" local response to the blocking of the alpha waves goes up to more than 100 milliseconds.

40. (*a*) Monnier, M., and Jeanneret, R.: Contrôle objectif de la conductibilité des voies optiques centrales par l'électro-rétinographie et l'électro-encéphalographie combinées, Ophthalmologica **113**:1-11, 1947. (*b*) Monnier, M., and Boehm, F.: Prüfung der Leistungsfähigkeit des optischen Systems durch kombinierte Elektroretinographie und Elektroencephalographie beim Menschen, Helvet. physiol. et pharmacol. acta **5**:C34-C35, 1947. (*c*) Monnier, M.: Mesure du temps rétinocortical à partir des potentiels corticaux évoqués par stimulation lumineuse chez l'homme, ibid. **6**:61-62, 1948.

41. Spielberg, P. I.: Electroencephalogram and Electroretinogram of Man, Eksper. biol. i med. **17**:35-37, 1944; footnote 13c.

Monnier [40c] referred to the central period as central transmission time. The prolongation of the blocking time at lower intensities is thought to be due to the (increased) latency of the peripheral processes. A comparison of the values for the latencies of the electroretinogram at those three intensities at which it has been technically possible to obtain electroretinographic tracings suitable for analysis gives a further criterion for this. The diagram in Figure 7 illustrates schematically, for these three intensities, the relation of the blocking time to that part which represents the latency of the electroretinogram. Thus, the prolongation of the blocking time corresponds to the prolongation of the latency of the electroretinogram.

Monnier and Boehm [40b] found the following values: retinal time, 65 ± 10 msec.; alpha-blocking time, 255 ± 60 msec.; central transmission time, 185 ± 60 msec. Figure 8 illustrates this.

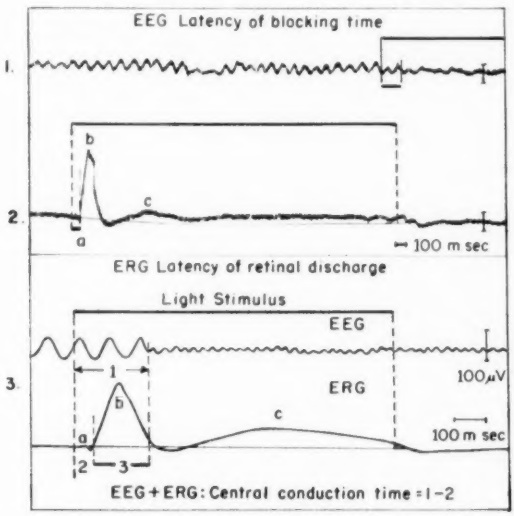

Fig. 8.—*1*, Electroencephalogram showing alpha rhythm and its suppression in course of stimulation with light; latency of alpha blocking time.

2, normal electroretinogram (H. M.) of temporal retinal field on stimulation with white light at 20 degrees (intensity, 0.1 lumen). Latency of retinal discharge of b-potential.

3, electroencephalogram and electroretinogram recorded simultaneously. Schematic demonstration of alpha rhythm-blocking time (*1*); latency of b-potential (*2*), and central conduction time (*3*). (Adapted from Monnier and Jeanneret,[40a] Fig. 1, p. 2.)

A comparison was made by Bernhard [40c] of the alpha-blocking time, the motor reaction time, and the electroretinogram. The muscle action currents were registered from the biceps when the subject, on seeing the light, quite slightly and rapidly bent the lower arm. This motor reaction took place after the blocking of the occipital alpha rhythm, as illustrated in Figure 9.

Owing to the difficulty in determining when the alpha rhythm stopped, at the suggestion of Grey Walter, Monnier [40] adopted as the criterion of cortical response the appearance of cortical rhythms evoked by light stimulation (photic driving), instead of the alpha rhythm. With his standard technique, these potentials, if they were present, appeared in normal subjects at 120 ± 25 msec. after the beginning of the light stimulus. By deducting from this time the latency of the retinal response,

70 ± 15 msec., one obtains the time of 50 ± 15 msec., which is more stable than the postretinal time of Bernhard, 165 ± 50 msec., and therefore a more adequate criterion for appreciation of the functioning of the optical pathway.

Monnier repeated these experiments, using a stroboscopic light and a six-channel electroencephalograph, in Grey Walter's laboratory. Stimulation was done with the patient's lids closed. The following figures were found in 47 experiments on three subjects: time necessary for the appearance of photic driving, 108 ± 15 msec.; latency of retinal response, 60 ± 15 msec.; retinal cortical time, 48 ± 10 msec.

VARIATIONS OF ELECTRORETINOGRAM WITH AGE AND SEX

During the first two or three days of life, according to Zetterström,[42] either there is no electroretinographic potential, or there is only a slight rise in the base line after each light stimulus. After a few days a distinctive, but not measurable, b-potential

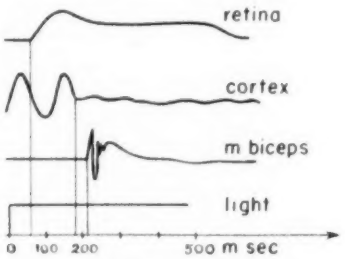

Fig. 9.—Diagram showing schematically the different responses from retina and cortex in relation to motor reaction (action potentials from right biceps) to light stimulus (*int. 1*). Time is expressed in milliseconds. Bernhard,[6e] p. 79.

appears. With this type of electroretinogram the latent period is prolonged to 0.06 second, and the duration of the b-potential, to 0.20 second. By the age of 3 months the b-potential is up to 0.10 or 0.20 mv with a latent period of 0.05 second and a b-potential duration of 0.16 second. At the age of 5 to 6 months the b-potential is up to 0.20 to 0.30 mv, with a latent period of 0.05 second and a duration of 0.16 second. During the second half-year there is no measurable increase in the size of the b-potential. At the age of one year the electroretinogram is of the adult type, but still remains somewhat subnormal in potential. There is no trace of an a-wave up to the age of one year. Zetterström suggests that this is due to the absence of the P III component.

Vainio-Mattila [43] compared the electroretinograms in men and in women of ages from 19 to 50. The series comprised 79 eyes, in 53 men, and 52 eyes, in 36 women. The average age was 29 years for the men and 31 years for the women. The results were as follows:

	Men	Women	Difference
B-Potential, mv	0.34	0.39	0.05
Latent period, sec.	0.04	0.04	0
Duration, sec.	0.15	0.15	0

42. Zetterström, B.: The Clinical Electroretinogram: IV. The Electroretinogram in Children During the First Year of Life, Acta ophth. **29**:295-304, 1951.

43. Vainio-Mattila, B.: The Clinical Electroretinogram: II. The Difference Between the Electroretinogram in Men and Women, Acta ophth. **29**:25-32, 1951.

The difference in the mean b-potential was the only difference in the two groups. One explanation might be that the smaller size of the female globe makes the electrode closer to the retina, giving a better leading off, which, in turn, gives a better conduction.

Karpe, Rickenback, and Thomasson [44] investigated the electroretinogram in 40 subjects above 50 years of age. The mean age was 57. The results were as follows:

B-Potential	0.32 mv	± 0.076
Duration, sec	0.16	± 0.021
Latency, sec	0.05	± 0.007

To determine whether there was a tendency toward diminished b-potential with increasing age, the group was subdivided into five subgroups. There was a decreased b-potential in each successive older age group. The group of 50 to 54 years showed a b-potential of 0.34 mv. Again, the female group showed a higher b-potential.

ABNORMAL FORMS OF THE ELECTRORETINOGRAM

According to Karpe [31] and Henkes,[45] there are four types of pathologic responses (Fig. 10): (1) An electroretinogram of subnormal size, to be referred to as "sub-

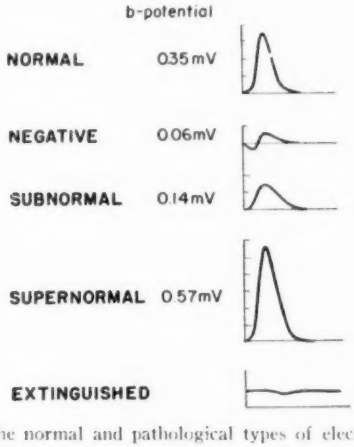

Fig. 10.—Diagram of the normal and pathological types of electroretinograms. Adapted in part from Henkes,[45] p. 597.

normal retinogram"; (2) a more or less pure negative response, "negative electroretinogram"; (3) no electric response, "extinguished electroretinogram," and (4) an electroretinogram of supernormal size, "supernormal electroretinogram."

The Subnormal Electroretinogram.—If one eye is normal, it is easy to state whether the electroretinogram from the diseased eye is of abnormal size. However, if the patient has only one eye, or if both eyes are affected, it is sometimes difficult to determine whether the electroretinogram is subnormal. Karpe [3] has derived a

44. Karpe, G.; Rickenback, K., and Thomasson, S.: The Clinical Electroretinogram: I. The Normal Electroretinogram Above 50 Years of Age, Acta ophth. **28**:301-306, 1951.

45. Henkes, H. E.: Use of Electroretinography in Disturbances of the Retinal and Choroidal Circulation, Proc. 16th Internat. Congress Ophth., London **2**:596-604, 1950.

formula to determine whether the b-wave recorded falls within or outside the normal range of variation. He found that the average duration of the subnormal electroretinogram is 0.13 second as compared with 0.15 second for the normal electroretinogram. No difference was found between the latent periods of the normal and the subnormal electroretinogram.

The Negative Electroretinogram.—The electroretinogram may become negative owing either to an increase in the negative component itself or to a diminution or delay of the positive P II component. This is the theoretical background for an interpretation of the pathologic negative electroretinogram in terms of its component potentials. It may or may not be possible to ascertain whether a given pathologic change is due to P II or P III.[3] Wirth [17] was doubtful as to whether a negative electroretinogram occurs. The negative electroretinogram, according to Karpe,[8] should have a diminished b-wave and an exceptionally well-marked negative a-wave, with preferably the negative component dominating in the rest of the electroretinogram.

Extinguished Electroretinogram.—The absence of a retinal electric response to illumination has been designated by the term "extinguished electroretinogram." There are eyes in which a certain amount of function has been preserved and the electroretinogram is unobtainable. An extinguished electroretinogram means that an electroretinogram either is totally lacking, so small as to be unrecordable, or that its two components have added up to zero.[3]

Wirth [17] believed that the extinguished electroretinogram means either that the potentials which were created by stimuli are below the threshold of our instruments or, less likely, that the positive and negative components have achieved a perfect equilibrium.

Supernormal Electroretinogram.—There are some cases in which the electroretinogram has been of supernormal size; i. e., it has fallen outside the normal limits of variation. Wirth [17] believes that for a supernormal retinogram to occur one would have to have variation in the blood composition, as suggested by Granit,[1] or that it might be due to a reorientation of the sources of the intraocular potentials, with a consequent redistribution of the internal resistance, so as to reduce the normal shunt of the intraocular liquids and tissues. It would be important in these cases to know the resting potential of the eye.

DISEASES IN WHICH THE ELECTRORETINOGRAM HAS BEEN RECORDED

Cataract.—Karpe and Vainio-Mattila [46] studied a group of 61 patients with cataract. The patients were divided into three groups: In the first group were 24 patients with no other disease found to affect the electroretinogram. The mean b-potential was 0.30 mv before operation, as compared with 0.28 mv after operation. Cataract led to prolongation of the b-potential, which the authors believed was due to the decrease in intensity of illumination on the retina caused by the cataract. They concluded from this that cataracts in general do not affect the b-potential of the electroretinogram, but do cause a slight increase in the duration and latency.

46. Karpe, G., and Vainio-Mattila, B.: The Clinical Electroretinogram: III. The Electroretinogram in Cataract, Acta ophth. **29**:113-128, 1951.

The second group included the first group as well as 33 others. Among the latter were patients with general disease, complicated cataract, and eyes with poor vision. Of these, eight had central choroiditis or macular holes; one had diabetic retinitis; in two choroidal detachment developed during the course of healing; one had postoperative retinal detachment, and one had iritis and secondary glaucoma after operation. The mean b-potential for this group was 0.30 mv before operation and 0.29 mv after operation.

The third group was made up of cataract patients with pathologic electroretinograms. Two patients had subnormal electroretinograms. The first patient had myopia and recurrent iritis, with a b-potential of 0.14 mv before operation, but vision of 0.9 after extraction. The other patient had a b-potential of 0.08 mv before extraction, and a choroidal sarcoma was found after extraction.

Two patients of the third group had a negative electroretinogram, but, in addition to cataract, these patients had siderosis. Six patients had extinguished electroretinograms. Of these patients, four had retinal detachments, one had retrolental fibroplasia, and one, a fresh embolism in the retinal artery.

Jacobson and O'Brien [33] studied the electroretinogram in 30 cases of cataract. In 27 of these a normal electroretinogram was recorded; in 12 cases a subnormal electroretinogram, and in 1 case an extinguished electroretinogram. The last patient had retinitis pigmentosa, and a poor postoperative visual result was obtained.

In a case of cataract owing to the diffuse irradiation of light and the greater absorption of light, the light intensity at the retina is decreased. In the case of uncomplicated cataract this absorption usually does not cause a lowering of the b-potential with 20 lux, but in the case of complicated cataract, in which more light is absorbed, 80 lux may have to be used, and sometimes this may not be sufficient. Thus, if a subnormal electroretinogram is recorded with an intensity of 20 lux, 80 lux should be used and the maximum b-potential considered representative of the function of the retina.[46]

Glaucoma.—Karpe [3] in 1945 recorded the electroretinograms of four patients with glaucoma. In one the electroretinogram was abnormal; in the remaining three it was normal. Leydhecker [47] recorded the electroretinograms from 73 glaucomatous eyes. The b-potential varied from 0.9 to 0.44 mv. There was no correlation between the b-potential and the field changes. Of the group with no field changes, 32% had a low b-wave potential, and 50% had a normal b-wave potential. Of the group with blind eyes, or vision limited to light perception, or perception of hand movements, or counting fingers, 43% had a low b-wave potential and 36% had a normal electroretinogram. There was a correlation between the size of the pupil and the b-potential. Of the group with a total iridectomy or a pupillary diameter of 4 mm. or over, a normal b-wave was obtained in 65% and a low b-wave potential in 12%. On the other hand, the reverse relation was found in eyes with a pupillary diameter of less than 4 mm. Of the eye with pupils of 4 mm. in diameter, eight were blind. In five of these a b-wave of greater than 0.30 mv was obtained with a stimulus of 20 lux, and in six, with a stimulus of 80 lux. There was no correlation between the ocular tension and the electroretinogram; neither was there any difference

47. Leydhecker, G.: The Electroretinogram in Glaucomatous Eyes, Brit. J. Ophth. **34:** 550-554, 1950.

between the cases of chronic simple and chronic congestive glaucoma. This would seem to indicate that the retinal action potential must originate deeper than the ganglion cells, which is consistent with the view that the b-wave is located in the bipolar cells.

Henkes [48] found normal electroretinograms in 60% and subnormal electroretinograms in 40% of the cases of primary glaucoma. He was of the opinion that the subnormal electroretinogram was found in all cases with sclerosis of the retinal vessels regardless of the primary process. It is known that vascular sclerosis may occur in primary glaucoma, and it is probable that the subnormal electroretinograms found in cases of glaucoma is due to such sclerosis.

Henkes [48] also noted that a decompression operation, such as an Elliot trephination, leads to a marked lowering of the b-potential, possibly as a result of changes in the blood flow through the vessels after operation. He believed that one may be faced with a new danger in the form of insufficient circulation in the retina after the hypertension has been abolished.

Circulatory Disturbances of the Retina.—In central-vein thrombosis all types of pathologic electroretinograms, except an extinguished type, have been recorded. In Karpe's [3] original series of five eyes, the prognosis was good and full restoration obtained in the two eyes which had supernormal or normal electroretinograms.

Henkes [49] distinguished three types of thrombosis of the retinal venous system: (*a*) thrombosis of the central vein; (*b*) thrombosis of one of the retinal veins, and (*c*) partial thrombosis of the central vein. He found that each of these clinical pictures corresponds with a significant type of electroretinogram. It would appear that a negative or subnormal electroretinogram in a case of thrombosis of the central vein tends to make the prognosis rather unfavorable. The eyes deteriorated whenever, during repeated examination, the b-potential of the retinogram decreased. Even under adequate treatment with such agents as anticoagulants and vasodilators, no improvement in this serious condition occurred except for subjective improvement in the visual acuity.

Both Karpe [50] and Henkes [51] concluded that the type of the electroretinogram found and the size of the b-potential are good indexes of the functional properties after recovery from the thrombosis.

Karpe [3] reported two cases with embolism of the retinal arteries. In the case of central embolism there was a subnormal electroretinogram, which probably had come from a small remaining viable part of the retina. In another case there was an embolus in a small arterial branch, and during the acute stage it presented an increased a-wave and a diminished b-wave. After healing the negativity disappeared, and the electroretinogram became identical with that of the patient's other eye.

In cases of periphlebitis retinae, a normal electroretinogram was found in the early stages. At this time the circulatory disturbance was limited to certain restricted areas. Either the normal parts of the retina had been large enough to

48. Henkes, H. E.: The Electroretinogram in Glaucoma, Ophthalmologica **121**:44-45, 1951.

49. Henkes, H. E.: The Electroretinogram in Thrombosis of the Vena Centralis Retinae, Ophthalmologica **121**:45, 1951.

50. Karpe, G.: Clinical Electroretinography, Tr. Ophth. Soc. U. Kingdom **69**:237-247, 1949; footnote 3.

51. Henkes, footnotes 45 and 49.

give a normal electroretinogram or the local deterioration may have been insignificant. However, in a case of advanced periphlebitis retinae with retinitis proliferans there was a definitely negative electroretinogram.[3]

Karpe [52] recorded the electroretinogram in cases of diabetic retinitis and found that it became pathologic only in the more advanced stages, when it became negative.

Henkes [53] studied the vasodilating effect of acetylcholine and benzazoline (priscol®) on two patients, one with general arteriosclerosis and the other with bilateral progressive "dystrophy" of the retina. In the first patient the affected, as well as the "normal" eye presented as subnormal electroretinogram. In the second patient, also, the electroretinogram was subnormal in both eyes. With acetylcholine the rise in the b-potential was only transitory, but with administration of benzazoline, if continued for three months, a normal b-potential was obtained. Henkes felt that, since the shape of the retinogram was largely dependent on the alterations in the blood circulation of the retina, the electroretinogram could be considered a most reliable indicator for study of the action of vasodilator drugs. One not only could decide which vasodilator is best, but, at the same time, could determine objectively the frequency of dosage and duration of action of the drug under consideration.

Macular Disease.—Karpe [3] studied three cases of macular disease in which the electroretinogram was normal. Two of these had acute central choroidretinitis, and the other heredomacular degeneration. An attempt was made to focus a 0.3-degree stimulus of 20 lux to the macular area after full correction of the refraction, but the electroretinogram remained normal. Riggs [54] observed two patients with marked foveal impairment, so that their central vision was poor. In these patients the electric responses on the stimulation of light were nearly normal.

Retinal Detachment.—The electroretinogram gives useful information regarding the prognosis of detachments, not only as to the possibility of reattachment, but also as to the visual result of operation. An eye with a very small b-potential is less likely to reattach on operation than is an eye with a more normal electroretinogram. Also, the larger and the longer-standing the detachment, the smaller the b-potential will be. It is also of great interest to find that in unilateral detachment even the other eye usually has a subnormal electroretinogram.[55] Jacobson and O'Brien [33] found in three cases of detachment that the prognosis might have been accurately gauged by the electroretinogram.

Retinitis Pigmentosa.—The typical electroretinogram in this disease is the extinguished form. Karpe [3] described a case with a subnormal electroretinogram, but in four other cases an extinguished electroretinogram was found. Jacobson and O'Brien [33] studied 20 cases of retinitis pigmentosa and found an extinguished electroretinogram in every one, regardless of the severity of the disease. Riggs [54] recorded the electroretinogram in three cases of this disease. The first

52. Karpe, G.: Clinical Applications of Electroretinography, Proc. 16th Internat. Congress Ophth., London **2**:591-595, 1950.

53. Henkes, H. E.: Use of Electroretinography in Measuring the Effect of Vasodilation, Angiology **2**:125-131, 1951.

54. Riggs, L. A.: Retinal Responses of Some Night-Blind Subjects as Measured Electrically, personal communication to the author.

55. Karpe.[3] Jacobson and O'Brien.[33] Karpe.[50] Karpe.[52]

represented an early stage of degeneration, and it was found that an intensity of approximately 2,000,000 foot lamberts was required to elicit even minimal responses from the retina. A second case, with more advanced disease, showed a small b-wave whose peak was reached 0.13 second after the onset of the flash of light, as compared with a time of 0.11 second for a normal subject. A third case represented a fairly advanced stage of retinitis pigmentosa in which foveal vision had also begun to suffer. In this case no electrical responses in the form of a b-wave were obtained.

Björk and Karpe [56] have found the electroretinogram to be a valuable aid in differentiating primary and secondary retinitis pigmentosa. They found the electroretinogram always extinguished in primary disease, while in secondary disease it was as a rule subnormal. In cases of very advanced secondary retinitis pigmentosa the electroretinogram may finally become extinguished.

Karpe [3] and Björk and Karpe [56] recorded the electroretinogram in a case of hemeralopia idiopathica hereditaria and found it to be extinguished. Riggs [54] also studied a congenitally night-blind subject. The electroretinogram in the dark-adapted state with an intensity 10 times normal resembled the records of normal subjects in the light-adapted state. There was a close agreement between the electrical data and psychophysical data with respect to both absolute sensitivity and the degree of dark adaptation.

Siderosis Retinae.—In general, the pathologic changes in the retina in siderosis retinae are similar to those seen in retinitis pigmentosa. The electroretinographic examination of patients with siderosis indicates that there is an initial stage of increased excitability of the retina, manifested by an increase in both the positive component of the retinogram (P II) and the negative one (P III). If the foreign body is extracted early enough, these changes may be reversible. This change takes place at such an early stage that examination by other clinical methods can give only an uncertain diagnosis. In the more advanced cases, the electroretinogram is negative, then extinct. This is probably due to degenerative changes in the retina.[57]

Optic Neuritis, Optic Nerve Atrophy, and Papilledema.—Karpe [3] recorded the electroretinogram in 10 cases of optic neuritis. The record was normal in the acute stage, as well as in the healed eye. He also recorded the electroretinogram in five eyes with partial or total optic nerve atrophy of the descending type and found it normal. François [58] found the electroretinogram normal in the following diseases of the optic nerve: degenerative disease, seven cases; inflammatory disease, six cases, and toxic, mechanical, or traumatic injury to the optic nerve, three cases. He believed that the electroretinogram remains normal regardless of the amount of atrophy of the nerve or change in the visual field. Even if the lesion is very old and accompanied by secondary or retrograde atrophy of the optic fibers and ganglion cells, the electroretinogram is normal. One can thus make a differential diagnosis of the ascending and the descending type of atrophy, since in the former the electroretinogram is altered, whereas in the latter it is unaltered.

56. Björk, A., and Karpe, G.: The Clinical Electroretinogram: V. The Electroretinogram in Retinitis Pigmentosa, Acta ophth. **29**:362-371, 1950.

57. Karpe, G.: Early Diagnosis of Siderosis Retinae by Use of Electroretinography, Docum. ophth. **2**:277-296, 1948.

58. François, J.: Premiers essais d'électro-rétinographie clinique, Ann. ocul. **185**:255-267, 1952.

Only one case of choked disk has been investigated, one in which the edema was caused by the metastasis of an adenocarcinoma in the right frontal lobe. The electroretinogram, as well as the vision, was normal.[3]

Avitaminosis A.—Björk and Gullberg recorded the electroretinogram in a case of avitaminosis A with night blindness. The record was of the photopic type on a recording made under standard conditions of dark adaptation. After disappearance of the avitaminosis A and development of normal light adaptation, the electroretinogram changed to the normal scotopic type.[52]

Strabismus.—Karpe [3] found the electroretinogram identical in the squinting amblyopic and in the normal eye. Keiner [59] recorded the electroretinograms of six children with strabismus. Anomalies in the electroretinograms could not be found in any of these patients, and the difference between the two eyes was not significant. Also, there was no difference in the electroretinogram when the temporal retina or when the nasal retina was stimulated.

High Myopia.—Karpe [3] found the electroretinogram to be subnormal in several cases of high myopia. There was also an extinguished electroretinogram in a case of high myopia with retinal detachment. François [58] recorded the electroretinograms in eight cases of high myopia, but found the results very variable.

COMMENT

According to Karpe,[3] analysis of the pathologic electroretinogram may be developed in two ways. First, the analysis may be developed as an interpretation in terms of the two components demonstrated by the electrophysiologic experiments, P II and P III. The second mode of analysis is to interpret the electroretinographic results from a more functional point of view (P II). Although the recorded electroretinogram represents a balance between P II and P III, it is safe to ascribe the whole gamut of changes from the supernormal to the negative electroretinogram to changes in P II, which, for the brief flashes used, finds its expression mainly in the b-wave. The negative electroretinogram, according to this mode of analysis, is the wave that remains upon removal or reduction of P II by a pathologic agent. Whether, in addition, the negative component is increased, normal, or diminished is a matter upon which it would be difficult to venture an opinion. Absence of response (extinguished electroretinogram) means that P II is greatly diminished. It is conceivable that in this case the P II and the P III components have struck a precise balance at zero potential, but this is unlikely as P II normally succeeds P III. For an extinguished electroretinogram to represent a perfect balance of P II and P III at zero potential, the latter component would have to be greatly delayed, as there is nothing to suggest that a pathologically reduced P II could be accelerated.

Unless very strong evidence can be adduced in favor of a change in the negative component, P III, it is sufficient, for practical purposes, to regard the pathologic types as caused by variations in the size of the positive component, P II, the negative component, P III, being the end-result of an excessive reduction of P II. In most,

59. Keiner, G. B. J.: New Viewpoints on the Origin of Squint, The Hague, Martinus Nijhoff, 1951.

if not in all, cases the extinguished electroretinogram should be regarded as a reduction below instrument threshold of both P II and P III. There are two factors which might produce an extinguished electroretinogram. First, some structure in front of, or at, the locus where potential is generated has been attacked by a pathologic agent. This could occur in a case of siderosis in which there is early degeneration of the two inner nuclear layers and the ganglion cells and later degeneration of the cones. Second, the potential changes are present, but have been short-circuited by some process in the retina or elsewhere in the globe.[60] Riggs [54] postulated that in retinitis pigmentosa the retinal degeneration associated with the puncture of the outer limiting membrane, the migration of pigment, and other abnormal conditions may have produced an electric "short circuit" that makes it impossible for a potential difference to be developed across the retinal layers. Karpe [57] stated that in siderosis that there might be formation of a shunt within the retina that prevents the recording of the potentials externally.

The electroretinogram, under the conditions used, must be regarded as a general response from the whole retina. It has been pointed out that in the opened, excised frog eye it is possible to obtain local responses from two adjacent stimulated spots if the stimuli are made very weak, so that the responses are of the order of 50 μv.[3] In Monnier's method of perimetric electroretinogram, although the stimulus size was 2 degrees, there was spread to the surrounding areas, as demonstrated by Fröhlich in 1914 in the retina of the octopus.[17] This suggests that in order to develop an electroretinographic method of perimetry it would be required to try to measure the light necessary for a threshold potential, and not the potential caused by a strong stimulus.[61]

The question of the control of the light stimulus must consider optical and electrophysiologic factors. The luminosity of the retinal image is determined by various conditions, the most important of which are the absorption, dispersion, and reflection of light in the media and, furthermore, the area of the pupil. In this connection, one must mention that the sensitivity of the retina depends on the direction of the incident light (Stiles-Crawford effect) and the position of the electrode. If the incident ray falls on the retinal area close to the electrode, a greater potential is developed than if the rays fall on a more distant area.[17] Fry and Bartley [62] stressed the importance of the nonfocal, or stray, light on the electroretinogram. They felt that the measured latency of the electroretinogram is that of the nonfocal b wave, and that variation in latency can be attributed to the change in quantity of stray light. Asher [63] found that if a light is focused on a blind spot, the resulting electroretinogram is as large as occurs when light is focused on another part of the retina.

Wirth [17] believed that the resting potential of the eye should be important in the human electroretinogram. This is made up of two factors, one being the metabolic activity of the visual cells (rods and cones), whose free ends are always negative

60. Karpe, footnotes 3 and 57.

61. Karpe,[3] Wirth.[17]

62. Fry, G. A., and Bartley, S. H.: Relation of Stray Light in the Eye to the Retinal Action Potential, Am. J. Physiol. **111**:335-340, 1935.

63. Asher, H.: Electroretinogram of the Blind Spot, J. Physiol. **112**:40P, 1951.

with respect to the base, and the other factor is the membrane potential between the blood and the aqueous. He believed that it would be of great value to know the resting potential, considering that it is due to the above two factors, especially the latter factor in glaucoma.

Noell [64] found that a rapid intravenous injection of small amounts of sodium azide produced an instantaneous and transient rise of the resting potential in animals. His experience seemed to indicate that the resting potential is the outcome of a complex function in which the activity of retinal metabolism and ion-transport processes between retina and extraretina participates.

In conclusion, Wirth [17] stated that the evaluation of the b-potential is not sufficient, so that the electroretinographic method gives us the desired help, and that for a more complete analysis we need an evaluation of the different components, an analysis of the resting potential and of its relation to P II, and the realization of a perimetric electroretinogram.

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64. Noell, W. K.: Electrophysiologic Study of the Retina During Metabolic Impairment, Am. J. Ophth. **35**(Pt. 2): 126-133, 1952.

Annual Reviews

LIDS, LACRIMAL APPARATUS, AND CONJUNCTIVA

Review of Recent Literature

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NEW ORLEANS

LIDS

CLONIC retraction of the upper lid associated with sucking was observed in an infant reported by Berkson.[1] A similar anomaly reported by Francheschetti in 1937 almost entirely disappeared in four years.

Hereditary bilateral ptosis, epicanthus, blepharophimosis, dystopia of the lower lacrimal puncta, and hypoplasia of the caruncles occurred in association with limitation of upward movement of the globes in a 3-year-old boy described by Klein.[2] The condition first appeared in the patient's grandfather, who transmitted it to five sons. A somewhat similar syndrome was described by Waardenburg[3] in 12 patients, who in addition were hereditary deaf-mutes. Raspidara[4] describes a patient with multiple congenital defects consisting of a palpebral coloboma with cutaneobulbar adhesions, coloboma of the eyebrow, ectopia of the superior lacrimal punctum and canaliculus, agenesis of the caruncle, plica semilunaris, and hypertrichosis of the forehead.

Pansini[5] offers as clinical evidence for the anatomical individuality of the nucleus of the levator palpebrae in the mesencephalon the case of a patient he observed with unilateral ptosis in whom the intrinsic and extrinsic ocular innervation was entirely intact on both sides and who subsequently suffered impairment of vision, manifestations of extrapyramidal type, and subjective disturbances in the form of frontal headaches.

The common dermatoses of the lid are listed by Zakon and Goldberg[6] as contact dermatitis, dermatitis medicamentosa, atopic eczema, impetigo, seborrheic dermatitis, herpes simplex, herpes zoster, congenital vascular and pigmented lesions, senile and seborrheic keratosis, epithelioma, xanthelasma, and milia. Less common dermatoses are verruca, molluscum contagiosum, vitiligo, angioneurotic edema, lupus erythematosus, syphilis, sarcoidosis, lupus vulgaris, erysipelas, radiodermatitis, purpura, melanoma, scars and keloids, granuloma pyogenicum, and lymphangioma.

From the Tulane University of Louisiana School of Medicine.

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2. Klein, M.: Hereditary Bilateral Ptosis and Blepharophimosis Associated with Other Developmental Abnormalities of the Outer Eye, Proc. Roy. Soc. Med. **43**:1025-1026, 1950.

3. Waardenburg, P. J.: A New Syndrome of Interest to Oculists and Otologists, Nederl. tijdschr. geneesk. **1**:58-59, 1952.

4. Raspidara, D.: A Rare Case of Palpebral Congenital Coloboma Associated with Numerous Anomalies, Resenha clín.-cient. **20**:229-233, 1951.

5. Pansini, A.: Clinical Individuality of the Nucleus of the Levator Palpebrae, Acta neurol. **5**:211-215, 1950.

6. Zakon, S. J., and Goldberg, A. L.: Dermatoses of the Eyelids, Eye, Ear, Nose & Throat Month. **30**:313-315, 1951.

Rare dermatoses are accidental vaccinia, solid edema, myxedema, benign tumors of congenital origin, cutaneous horns, xeroderma pigmentosum, idiopathic multiple hemorrhagic hemangioma of Kaposi, varicelliform eruption, primary inoculation tuberculosis, tuberculosis disseminata facei, lichen nitidus, blastomycosis, dermatomyositis, and leprosy.

In reporting a case of primary pyodermatitis vegetans of the eyelid probably caused by cocci, Azzolini [7] emphasizes the rapidity of appearance and evolution of the clinical signs as compared with those of other ulcerating processes of the skin of the lids.

Inflammatory lesions of lids are rarely complicated by cavernous sinus thrombosis; however, Moser [8] observed hordeolum develop into orbital cellulitis and cavernous sinus thrombosis in four cases. In each case penicillin and a sulfonamide were given and the orbit was exenterated. Two patients recovered, and two died.

Habresin and Bernolet [9] observed the development of vaccinial pustules in the lids and conjunctiva in association with corneal ulcers in a man aged 60. The lesions were thought to be endogenous and to follow vaccination. However, Shemeley [10] reports a case of bilateral vaccinial infection of the lids and conjunctiva which resulted from manual transmission of the virus.

Although fungous infection of the lids is rare, Mariotti [11] reports a case of trichophytosis of the eyebrow, and Chan,[12] a case of trichophytosis of the lower lid margin associated with fine, diffuse superficial keratitis of the lower third of the cornea.

Voisin and Bismut [13] removed a 1-cm. piece of spectacle glass which had been in the eyebrow of a young woman for 16 years, after a fall from a bicycle. Attacks of pain, swelling, and spontaneous ecchymoses had occurred at two- or three-year intervals.

Slate-gray pigmentation of the skin of the lids following prolonged use of mercurial ointments is reported by Long and Danielson.[14] Minute granules giving a presumptive reaction for mercury were found in large numbers in the cutis, and quantitative tests revealed mercury in the skin. The pigmentation faded after use of the ointment was stopped.

Allergy, according to Barraquer,[15] should be considered not as a unique uniform phenomenon, but as a complex encompassing various pathogenic, etiologic, immuno-

7. Azzolini, U.: Single Focus of Primary Pyodermatitis Vegetans of the Eyelid, Gior. ital. oftal. **4**:81-85, 1951.

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14. Long, J. C., and Danielson, R. W.: Mercurial Discoloration of the Eyelids, Am. J. Ophth. **34**:753-756, 1951.

15. Barraquer, T.: Nonspecific Allergy, Arch. Soc. oftal. hispano-am. **10**:1303-1309, 1950.

logic, and clinical forms. In discussing the pathogenesis in various cases of nonspecific ocular allergy, the author assumes that irreversible changes had occurred in the vascular walls. In this connection he refers to the so-called collagen diseases and suggests that the relation of these diseases to vernal conjunctivitis be investigated.

Eidelman [16] emphasizes that allergic inflammation of the skin of the lids and face may develop during treatment of diseases of the eye and that a generalized cutaneous hypersensitivity always was associated, since patch tests of a healthy part of the skin usually revealed the offending agent in 24 hours. Such a sensitivity reaction developed after the use of antistine® (2-[N-phenyl-N-benzylaminoethyl]-imidazoline) eye drops for one week in one case and after a year in two cases reported by Guerrant and Hollifield.[17] Patch tests gave strongly positive reactions in all three cases. Egan [18] observed the development of dermatitis of the lids following an intramuscular injection of penicillin in oil in a patient who had previously had a dermatitis of the lids from the application of penicillin ointment.

By means of arteriography Banquero-Gonzalez [19] localized a cirsoid aneurysm in the right lower lid. The tumor was removed through an infraorbital incision parallel to the lid after ligation of the external carotid artery.

Rudolph [20] describes a squamous-cell carcinoma which appeared in the region of the right tear sac in 1948 in a patient who had been examined after the injection of a thorium contrast fluid in both sacs in 1931. The skin over the left tear sac was indurated and retracted but not carcinomatous.

Adenocarcinoma of the Meibomian glands is described in a man aged 73 by Helmy Ibrahim.[21] After excision of the tumor the patient received radiation therapy. This type of malignant tumor is rare.

Reeh and Swan [22] report that many so-called rodent ulcers actually arise from the embryonic forms of skin adnexa, such as hair follicles and sebaceous and sudoriferous glands. Characteristically these tumors occur in the lower lid near the inner canthus. They have an elevated, telangiectatic border around a central portion, which is subject to recurrent ulceration.

The chemosurgical treatment of epitheliomas of the lids is advocated by Schreus.[23] After excochleation with a sharp spoon, the remaining tumor tissue is cauterized with zinc chlorate. Good cosmetic and functional results were obtained even in extensive lesions because the method did not sacrifice more tissue than necessary. In rare cases the author considers additional radiation therapy.

16. Eidelman, B. M.: Skin Tests in Diagnosis of Allergic Dermatitis Medicamentosa, Vestnik oftal. **29**:16-17, 1950.

17. Guerrant, J. L., and Hollifield, W. C.: Palpebral Dermatitis Following Use of Antistine Eyedrops, Am. J. Ophth. **34**:1318-1320, 1951.

18. Egan, J. A.: Localized Sensitivity of Eye to Penicillin, Am. J. Ophth. **34**:289-290, 1951.

19. Banquero-Gonzalez, R.: Cirsoid Aneurysm of the Right Lower Eyelid, Bol. Soc. venezol. cir. **3**:183-188, 1950.

20. Rudolph, H.: Development of Carcinoma of the Eyelid Long After Injection of Thorium, Beitr. path. Anat. **111**:158-164, 1950.

21. Helmy Ibrahim, A.: Adenocarcinoma of the Tarsal Glands (Meibomian), J. Roy. Egyptian M. A. **34**:42-44, 1951.

22. Reeh, M. J., and Swan, K. C.: Experiences with Tumors of the Lid, Tr. Am. Acad. Ophth. **54**:312-325 (March-April) 1950.

23. Schreus, T.: Chemosurgical Treatment of Epithelioma of the Eyelids, Klin. Monatsbl. Augenh. **118**:397-400, 1951.

Rossitto [24] and Greve,[25] on the other hand, advocate contact x-ray therapy for epithelioma of the lids. Rossitto advocates repeated treatments over a period of one to two months, with a total dose of 5,000 to 8,000 r, and Greve advises a dose of not less than 6,000 r. Rossitto reports excellent results in 14 cases, but in 4 others supplementary radium therapy had to be applied. Greve records only 1 relapse in 75 cases; he reports cures in only 68, or 90.7%.

Lo [26] reports three unusual cases of divided nevus of the lids which raise the question whether the origin of division of such nevi is always to be traced to intrauterine life.

A large pretarsal sarcoma of the left upper lid in a woman aged 73 is reported by Beaujon.[27] No metastasis was found one year after exenteration of the orbit, followed by x-ray therapy.

A tumor removed from the supraorbital region of an 8-year-old child proved to be a plexiform neurinoma, according to Jacobius and Leubarg.[28] The tumor reappeared in five months and, upon removal, revealed the same type of histological structure. Although apparently excised completely, the mass recurred a third time within one year.

Blepharochalasis of 15 years' duration in a man aged 53 was corrected by excision of the redundant skin and subcutaneous tissue with fixation of the lower margin of the wound to the upper margin of the tarsus. Microscopic examination of the excised tissue, according to Titche and O'Connor,[29] revealed the vessels of the corium to be increased in number and surrounded by inflammatory cells, predominantly lymphocytes, with occasional plasma cells, eosinophiles, and polymorphonuclear leucocytes.

The primary cause of senile entropion, according to Fox,[30] is the degeneration of tissues and absorption of orbital fat. The spastic element is a secondary factor, resulting from corneal irritation by the misplaced lid. Therefore he devised a technique of correction based upon strengthening of the tissues by vertical resection. He excised a triangular piece of the tarsoconjunctival layer of the lid. The apex of the triangle was at the lid border, and the base, 5 mm. wide, at the attached border of the tarsus. In addition, he removed a spindle-shaped piece of tissue from the skin and muscle layers of the lid just below the outer canthus. The spindle measured 15 mm. vertically and 8 to 10 mm. horizontally at its widest point. The tarsal incision was closed with interrupted 4-0 braided black nonabsorbable surgical (silk) sutures, and the skin incision, with interrupted 5-0 silk sutures. The operation was successful in 14 lids of 10 patients, without recurrence after 2 to 20 months.

For cicatricial entropion, Rappaport [31] recommends a modification of Ewing's operation. However, Djacos [32] warns that the conjunctiva should be preserved and

24. Rossitto, R. M.: Roentgen Contact Therapy in Treatment of Epithelioma of the Eyelid, Arch. ottal. **54**:151-162, 1950.

25. Greve, W.: X-Ray Therapy of Lid Cancer, Klin. Monatsbl. Augenh. **118**:391-397, 1951.

26. Lo, W. B.: Divided Nevus of the Eyelid, Chinese M. J. **69**:258-261, 1951.

27. Beaujon, O.: Sarcoma of the Eyelid, Rev. policlin., Caracas **19**:37-54, 1951.

28. Jacobius, H. F., and Leubarg, M.: Plexiform Neurinoma of the Left Supraorbital Region, Am. J. Ophth. **34**:1177, 1951.

29. Titche, L. L., and O'Connor, M. J.: Blepharochalasis, Am. J. Ophth. **34**:1314-1316, 1951.

30. Fox, S. A.: Relief of Senile Entropion, A. M. A. Arch. Ophth. **46**:424-431, 1951.

31. Rappaport, O. C.: Operative Treatment of Cicatricial Entropion in Trachoma in the Tropics, Ophthalmologica **212**:221-224, 1951.

32. Djacos, C.: Entropion and Trichiasis: Solution of the Surgical Problem, Ann. ocul. **183**:943-956, 1950.

that when the entropion is combined with trichiasis, even if partial, a strip of skin and tarsus 3 to 4 mm. wide should be excised from the whole length of the lid. The desired effect was regulated by the amount of upper tarsal lip included with a continuous absorbable surgical (gut) suture.

Charamis [33] reports the successful treatment in five cases of cicatricial ectropion of the lids by the transplantation of a free cutaneous graft taken from the abdominal skin with a Padgett dermatome. However, Ferrié [34] used a flap technique for ectropion following burns of the face. After freeing of the lid and tarsorrhaphy, a flap was outlined by a curvilinear incision, beginning at the nasal extremity of the denuded surface and swinging back nearly to the inferior part of the tragus, then extended by a linear incision toward the center of the cheek. The flap was rotated and sutured to cover the lid defect. Two days later the triangular defect in front of the tragus was covered with Davis grafts.

In a man aged 45 who had been virtually blind for seven years because of intractable blepharospasm, Fox [35] removed a broad band of orbicularis fibers extending from the upper orbital margin halfway down the upper tarsus on each eye. The result was eminently satisfactory, since lid closure was normal except for fleeting periods of tonic blepharospasm.

The most frequent cause of the deformity known as bags of the eyelids was found to be herniation of the orbital fat by Castanares,[36] who advocates removal of redundant skin and excision of the accumulations of herniated fat.

Various methods of repair of full-thickness defects of the lid have been described recently. Knaibl [37] made a skin flap with a pedicle from the forehead which he lined with a free mucus membrane graft from the lower lip. After three weeks the flap was turned into the defect of the lid. The pedicle was severed after another three weeks, and a month later the flap was remodeled into final form and size. Kamel [38] used a sliding flap from the skin of the temple to repair the defect of an upper lid after removal of an adenocarcinoma of the Meibomian gland. For a larger defect in an upper lid, Callahan [39] used a full-thickness segment, 11 by 8 mm., from the opposite upper lid. In making the excision, he offset the incisions for the anterior and posterior laminas 2 mm. to permit closure by the halving principle. A new method for the lower lid devised by Manchester [40] consisted of mobilizing a conjunctival flap corresponding in width to the defect from the lower fornix and bulbar conjunctiva and covering it with a double-pedicled skin flap from the upper lid.

33. Charamis, J.: A Series of Blepharoplasties with Free Skin Grafts Taken with Padgett's Dermatome, Bull. Soc. héllén. opht. **18**:89-93, 1951.

34. Ferrié, J.: Correction of Cicatricial Ectropion of the Inferior Eyelids in Extensive Burns of the Face, Arch. opht. **11**:52-54, 1951.

35. Fox, S. A.: Relief of Intractable Blepharospasm: A Preliminary Report, Am. J. Ophth. **34**:1351-1356, 1951.

36. Castanares, S.: Blepharoplasty for Herniated Intraorbital Fat: Anatomical Basis for a New Approach, Plast. & Reconstruct. Surg. **8**:46-58, 1951.

37. Knaibl, P. V.: Plastic Surgery of the Upper Eyelid, Arch. urug. med. **38**:51-54, 1951.

38. Kamel, S.: Partial Resection of the Upper Eyelid and Its Repair, Brit. J. Ophth. **35**:377-379, 1951.

39. Callahan, A.: The Free Composite Lid Graft, A. M. A. Arch. Ophth. **45**:539-545, 1951.

40. Manchester, W. M.: A Simple Method for the Repair of Full Thickness Defects of the Lower Lid, with Special Reference to the Treatment of Neoplasms, Brit. J. Plast. Surg. **3**:252-263, 1951.

In cases of scars in the upper fornix, narrowing of the palpebral fissure was accomplished by Pavisic [41] through lengthening of the levator muscle by grafting a strip of oral mucosa between the recessed levator tendon and the upper tarsus.

LACRIMAL APPARATUS

In considering the functions of the lacrimal apparatus, Markovitch [42] found a division into three parts: a secreting, an intermediate, and an excreting part preferable to division into classic secreting and excreting parts. He points out that the important functions actually take place in the intermediate part. He calls attention to the importance of the secretion of the accessory glands, as well as to the action of the lids and osmotic phenomena of the surface of the cornea in elimination of tears in this intermediate space.

The average level of glucose in the tears was found by Giardini and Roberts [43] to be 2.5 mg. per 100 ml. This figure represented only 40% of the total reducing substance content of tears, as compared with 80% of the total for blood. They also found that the chloride content of the tears fell from 135.5 to 110.4 mM. per liter after prolonged lacrimation. In contrast, Balik,[44] using Votocek's method of analysis, found that the chloride concentration was highly independent of the quantity of tear secretion.

A boy aged 10 years was found to have a cystic enlargement of the upper canaliculus in association with a subconjunctival chondroma and congenital coloboma of the upper lid (Jaensch [45]).

Puncta were present, but divided by a central caruncle, in six patients with cyclopia examined by Morton.[46] Lacrimal sacs were not found.

Acute unilateral dacryoadenitis was observed by Wilson [47] in 4 patients in the course of six months, and among *3,622* new ophthalmologic patients. The patients, two boys and two girls, were 10 to 16 years of age. Each had had a preceding respiratory infection, followed by swelling of the upper lid, proptosis, and chemosis of the conjunctiva. Limitation of rotation of the globe with some diplopia occurred in two cases. As the swelling diminished under penicillin and sulfanilamide therapy, a mass was palpated in the lateral part of the upper lid. The differential diagnosis included orbital cellulitis, osteitis, and septic chalazion. The author considered tenderness over the malar bone an early sign of acute dacryoadenitis.

41. Pavisic, Z.: Operative Narrowing of the Eyelids, Ophthalmologica **123**:57-59, 1952.

42. Markovitch, A.: Considerations on the Division of the Lacrimal Apparatus, Ann. ocul. **184**:803-810, 1951.

43. Giardini, A., and Roberts, J. R. E.: Concentration of Glucose and Total Chloride in Tears, Brit. J. Ophth. **34**:737-743, 1950.

44. Balik, J. I.: Quantitative and Qualitative Examination of the Tears, Československ oftal. **7**:305-314, 1951.

45. Jaensch, P. A.: Subconjunctival Chondroma in Congenital Coloboma of the Superior Lid Associated with Malformation of the Lacrimal Canaliculus, Klin. Monatsbl. Augenh. **117**:615-620, 1950.

46. Morton, W. R.: Lacrimal Channels in Cyclopia: An Investigation of Their Presence in the Specimens in Ireland, Ulster M. J. **20**:189-194, 1951.

47. Wilson, P.: Acute Unilateral Dacryoadenitis: A Report of 4 Patients, Brit. M. J. pp. 1183-1185, 1951.

Shaffer and Ridgway [48] observed permanent obstruction of the tear passages in cases of glaucoma treated with 10% furtrethonium (furmethide®) iodide for more than three months. The first symptoms were profuse tearing. The stenoses most frequently were in the canaliculi and usually were multiple. Bacteriologic examinations did not reveal a cause. Histologic examinations revealed nonspecific granulation tissues.

Dobromilsky and Mogilevskaja [49] were successful in establishing drainage in 15 of 23 cases of congenital dacryostenosis by retrograde probing. Their successes were higher in younger children, there being five cures in six infants under 4 months of age.

In the medical treatment of chronic dacryocystitis Colombo [50] advises elimination of infection, instillation of ischemia-producing collyria, and, finally, if the desired results are not obtained, repeated probings at intervals of at least three days.

McGovern [51] investigated the rhinologic aspects of 25 cases of chronic dacryocystitis. He found chronic suppurative sinusitis in three and atrophic rhinitis in two, but nasal defects were significantly absent. However, he emphasizes the necessity of making a complete rhinologic examination before contemplating operation.

Engel [52] reports five cases of unilateral epiphora without apparent cause, but in which careful examination revealed a slight eversion of the lower punctum. The epiphora was relieved by Hoffmann's method of excision of a small triangle from the posterior canalicular wall.

Abel [53] observed a hemorrhage without apparent cause from the lacrimal punctum of a 78-year-old, ruddy-complexioned, heavy-drinking man.

Two months after being exposed to infection with tuberculosis, a 5-year-old girl had swelling of a preauricular gland and dacryocystitis. Huggert [54] demonstrated tubercle bacilli from the lacrimal sac and cervical glands, although the conjunctiva on the side of involvement was normal. The disease progressed slowly to fistula formation until dihydrostreptomycin was used to control the infection, and one year later a successful dacryocystorhinostomy was made. A somewhat similar tuberculous infection of the nasolacrimal duct was observed by Konstam and Meynell [55] in a 14-month-old infant. The infection probably was primary in both cases, since tuberculous lesions were not found elsewhere.

An injury to the right lacrimal sac by a piece of wire produced a lacrimal fistula in a 52-year-old longshoreman. When conservative measures failed, Chervin [56] brought about relief with a dacryocystorhinostomy.

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48. Shaffer, R. N., and Ridgway, W. L.: Furmethide Iodide in the Production of Dacryostenosis, Am. J. Ophth. **34**:718-720, 1951.

49. Dobromilsky, F. I., and Mogilevskaja, F.: Treatment of Dacrocystitis in Infants and Young Children by Retrograde Probing, Vestnik oto-rino-laring. **4**:54-56, 1950.

50. Colombo, G. L.: Medical Treatment of Chronic Dacryocystitis, Boll. ocul. **29**:603-608, 1950.

51. McGovern, F. H.: Rhinological Aspects of Chronic Dacryocystitis, Virginia M. Month. **78**:74-76, 1951.

52. Engel, S.: One-Sided Epiphora, Am. J. Ophth. **34**:444-446, 1951.

53. Abel, S.: Haemorrhage from the Lacrimal Punctum, Brit. J. Ophth. **34**:754-755, 1950.

54. Huggert, A.: A Probable Case of Primary Tuberculosis of the Lacrimal Sac, Acta ophth. **29**:339-346, 1951.

55. Konstam, P. G., and Meynell, M. J.: Tuberculosis of the Nasolacrimal Duct, Lancet **1**:443-444, 1951.

56. Chervin, M.: An Infrequent Accident Caused by Working Conditions, Arch. Soc. oftal. litoral **3**:346-349, 1950.

A malignant tumor of the lacrimal gland was found by Charamis[57] to be the cause of unilateral progressive exophthalmos in a 57-year-old woman who had undergone mastectomy because of a tumor five years previously.

An adenoid cystic epithelioma of the lacrimal gland, salivary-gland type, which had existed for seven years in a man aged 70, was repeatedly excised but finally gave rise to widespread metastases to the pleura, lungs, and lymph nodes (McKinney and Butz[58]).

A mixed primary adenocarcinoma of the lacrimal gland was observed in four cases by Irvine, Roberts, and Soudakoff.[59] They conclude that these tumors eventually recur and frequently tend to become malignant and that therefore they must be removed early.

In the case of prelacrimal tumors, Radnot and Remenar[60] advise that an x-ray examination of the lacrimal sac usually permits a correct diagnosis, so that the tumor can be removed without injury to the sac.

Brand[61] successfully treated a polypus of the lacrimal sac by dacryocystorhinostomy. The diagnosis was suspected because the swelling in the lacrimal region was more elastic and of greater consistency than a mucocele of the sac. The small amount of fluid that regurgitated was not consistent with the size of the swelling, and after expression of the contents and syringing of the sac several bloody drops appeared in the nose. Finally, after these manifestations the swelling was unchanged. The tumor was attached by a small pedicle in the nasolacrimal duct and nearly filled the sac. It was a fibroma laxum.

Ashton, Choyce, and Fison[62] reviewed the 73 cases of primary tumor of the lacrimal sac reported up to 1950 and reclassified these tumors as epithelial and nonepithelial. Analysis showed that 50% fell into the papillocarcinoma group, and the authors emphasize the necessity for careful histologic examination of all lacrimal tumors, even though the clinical findings do not suggest malignancy.

A bilateral reticulum-cell carcinoma arising from the region of the lacrimal sac in a woman aged 64 is reported to have caused the death of the patient within 16 months of the first appearance of symptoms (Linoli and Bocci[63]).

A new method of closure of the lacrimal punctum is presented by Tóth,[64] who excised the punctum with a 1.5 mm. trephine, curetted the entrance of the canaliculus, and closed the wound with two sutures.

57. Charamis, J.: Malignant Tumor of the Lacrimal Gland, Bull. Soc. héllén. opht. **18**:96-97, 1950.

58. McKinney, W. W., and Butz, W. C.: A Mixed Tumour of the Lacrimal Gland with Extensive Metastases, Am. J. Ophth. **34**:1519-1524, 1951.

59. Irvine, R. A.; Roberts, W. L., and Soudakoff, P. S.: Tumor of the Lacrimal Gland: Report of 4 Cases, Am. J. Ophth. **34**:1511-1519, 1951.

60. Radnot, M., and Remenar, L.: Contribution to Diagnosis of So-Called Prelacrimal Tumors, Klin. Monatsbl. Augenh. **118**:78-80, 1951.

61. Brand, I.: Symptomatology of and Operation on Polypi of the Lacrimal Sac, Klin. Monatsbl. Augenh. **118**:172-175, 1951.

62. Ashton, N.; Choyce, D., and Fison, L. G.: Carcinoma of the Lacrimal Sac, Brit. J. Ophth. **35**:366-376, 1951.

63. Linoli, O., and Bocci, G.: Reticulum-Cell Sarcoma Involving the Lacrimal Sac: A Pathologic and Clinical Study, Boll. ocul. **30**:65-98, 1951.

64. Tóth, Z.: A New Method to Close the Lacrimal Punctum, Klin. Monatsbl. Augenh. **117**:521-524, 1950.

In a survey of teaching centers, Jones and Boyden[65] found that 90% of all dacryocystorhinostomies were made through an external approach. However, they prefer the intranasal route and list the following advantages: lack of external scar, no hematoma, avoidance of injury to the eye, and absence of orbital cellulitis or abscess. They report 64 cases in which the method was unattended by failure.

Christensen[66] devised a plastic nasolacrimal probe, comparable to a No. 3 Bowman probe, which was attached to a light source. When introduced into the lacrimal sac, the light was readily seen in the nasal cavity, marking the site for incision and entrance into the lacrimal fossa.

Comprehensive papers on external dacryocystorhinostomy have been published recently by Rycroft,[67] Valière-Vialeix,[68] Heinsius,[69] Wilde,[70] Belmonte González,[71] Aalde,[72] Gill and White,[73] Caballero del Castillo,[74] and Sayed.[75] All these brought out the well-known technical features of the operation which insure its success.

Brand[76] reports that naphazoline (privine®) hydrochloride U. S. P. added to the local anesthetic, as well as applied as drops into the wound, proved to be useful in lessening the hemorrhage in the various stages of the operation.

Klemens[77] found that a trephine whose edge and outer wall were coated with diamond dust was more useful and did not injure the nasal mucosa.

From x-ray studies of the opening made a year after external dacryocystorhinostomy in 46 cases, Stefek[78] concludes that it contracts only slightly when it has been made sufficiently large.

Ertel[79] reestablished drainage in cases of stenosis of the lower end of the lacrimal sac by opening the sac, curetting the stenosis, and inserting a "supramid" tube into

65. Jones, L. T., and Boyden, G. L.: The Rhinologist's Role in Tear Sac Surgery, Tr. Am. Acad. Ophth. **55**:654-661 (July-Aug.) 1951.

66. Christensen, L.: Localization of Lacrimal Sac in Dacryocystorhinostomy by Transillumination, A. M. A. Arch. Ophth. **46**:501-503, 1951.

67. Rycroft, B. W.: Surgery of External Rhinostomy Operations, Brit. J. Ophth. **35**:328-338, 1951.

68. Valière-Vialeix: Dacryocystorhinostomy: Indications, Technique, Results, and Obstacles, Based on 25-Years' Personal Experience, Ann. ocul. **184**:504-521, 1951.

69. Heinsius, E.: Treatment of Stenosis and Obliteration of the Lacrimal Passage, Klin. Monatsbl. Augenh. **117**:524-529, 1950.

70. Wilde, N. J.: Dacryocystorhinostomy, Plast. & Reconstruct. Surg. **8**:234-236, 1951.

71. Belmonte González, N.: Essentials and Matters of Secondary Importance in Dacryocystorhinostomy, Arch. Soc. oftal. hispano-am. **11**:113-121, 1951.

72. Aalde, O.: Dacryo-Cysto-Rhinostomy: An Analysis and Follow-Up of 338 Operations, Acta ophth. **28**:523-540, 1950.

73. Gill, E. G., and White, F. D.: Surgical Treatment of Chronic Dacryocystitis: Toto-Mosher Operation, Eye, Ear, Nose & Throat Month. **30**:197-199, 1951.

74. Caballero del Castillo, D.: Our Technique in Dacryocystorhinostomy, Medicamenta **9**:197-200, 1951.

75. Sayed, R. A.: A New Technique of Dacrocystorhinostomy, Medicus **2**:46-47, 1951.

76. Brand, I.: Control of Bleeding Dacryocystorhinostomy, Ophthalmologica **121**:217-220, 1951.

77. Klemens, F.: Dacryocystorhinostomy by Toti's Method, Klin. Monatsbl. Augenh. **118**:401, 404, 405, 1951.

78. Stefek, J.: Control of Osteotomy Opening in Dacryocystorhinostomy, Československ. oftal. **7**:33-36, 1951.

79. Ertel, R.: Experiences with Implantation of a Small "Supramid" Tube for Relief of Stenosis of the Lacrimal Sac, Klin. Monatsbl. Augenh. **119**:140-146, 1951.

the nasolacrimal duct. The incision in the sac was closed with absorbable surgical sutures. Similar procedures are described by Rolf and Jackson,[80] who used a tantalum or stainless steel cannula, and by Gay,[81] who used a vitallium* tube.

When lacrimal sac and canaliculi both were absent, Rycroft[67] successfully reestablished drainage by canthorhinostomy, grafting a tube of buccal mucosa between the conjunctival fornix and the nasal cavity.

In a patient with an incomplete extirpation of the lacrimal sac, with a fistula in the scar, Fronimopoulos[82] established drainage into the nose by an external rhinostomy and passage of a heavy absorbable surgical suture through the lower punctum and into the nose.

In six cases of epiphora following radiation therapy of carcinoma of the lids, with cicatricial involvement of the lacrimal passages, Cavalheiro Wilimersdorf[83] obtained relief from tearing and improvement of the scarring after excision of the lacrimal gland, whereas Hynie[84] reports good results in 92% of 78 patients with intractable epiphora who were treated by electrocoagulation of the palpebral part of the lacrimal gland.

A simple and effective operation for correction of eversion of the punctum was devised by Lee.[85] A triangular piece of skin was removed from the inner canthus and the defect closed by a sliding flap made at the inner portion of the lower lid.

CONJUNCTIVA

Three types of aneurysm of conjunctival vessels were found by Weinstein and Forgacs[86]: saccular, usually situated at bifurcations, occurring in arteriosclerosis; fusiform, occurring in hypertension, and berry-shaped, occurring mainly in diabetes. All three types, however, were found in healthy persons, the incidence increasing with the age of the patient. In some instances a saccular aneurysm changed into the fusiform type within a week.

Biomicroscopic examination of the conjunctival veins revealed the presence of white balls as the sign of leukergy in vivo in 31 patients with various febrile diseases (Dymitrowska[87]).

With high-power biomicroscopic examination of the normal conjunctiva, Lowenstein[88] observed very fine capillaries, some clear and glass-like, with no red blood

80. Rolf, D. E., and Jackson, C. C. R.: A New Tear-Sac Cannula for Dacryocystorhinostomy Operations, Am. J. Ophth. **34**:293-295, 1951.

81. Gay, E. C.: Dacryocystoblennorrhea with Hare Lip and Cleft Palate, M. Radiog. & Photog. **21**:23-25, 1951.

82. Fronimopoulos, J.: Treatment of Epiphora After Extirpation of the Tear Sac, Klin. Monatsbl. Augenh. **118**:528-530, 1951.

83. Cavalheiro Wilimersdorf, J.: Extirpation of the Lacrimal Gland in Patients with Epiphora Caused by Cicatrization of Irradiated Carcinoma, Arch. brasil. oftal. **14**:43-46, 1951.

84. Hynie, J.: Electrocoagulation of the Lacrimal Gland in Epiphora, Československ. oftal. **7**:337-370, 1951.

85. Lee, O. S.: Operation for Correction of Everted Lacrimal Puncta, Am. J. Ophth. **34**:575-578, 1951.

86. Weinstein, P., and Forgacs, J.: Conjunctival Angioscopy, Brit. J. Ophth. **35**:479-483, 1951.

87. Dymitrowska, M.: Biomicroscopic Research in Leukergy, Ann. Univ. Mariae Curie-Sklodowska **4**:625-632, 1949.

88. Lowenstein, A.: Closed Branches of Conjunctival Vessels, Brit. J. Ophth. **35**:595-600, 1951.

cells, and others with single red cells. Microscopic studies of stained sections revealed some collapsed branches, some twigs filled with endothelial cells, and some with single lymphocytes. Some branches were controlled by sphincter muscles in the conjunctiva, but cushion cells were not found.

Comparative measurements of the pressure in conjunctival veins and aqueous veins were made by Linnér, Rickenbach, and Werner.[89] By means of a torsion balance the pressure in the aqueous veins was observed to average 10.05 mm. Hg and that in the conjunctival veins, 9.04 mm. Hg, but with a pressure chamber the average was 11.40 mm. Hg for the aqueous veins and 12.14 mm. Hg for the conjunctival veins.

Minute cystoids, or vacuoles, were found by Trantas[90] in the bulbar and palpebral conjunctiva of normal persons, as well as of a patient with iritis and one with trachoma.

Experimental studies by Bocci[91] showed that the conjunctival mucosa can absorb antigens. A local immunity was produced by instillation of antigen for a short time, four to eight days, whereas general immunity followed prolonged instillations.

Bacteriologic studies of inflammatory lesions of the lid and conjunctiva, made by Pritikin, Duchon, and Farmer,[92] revealed that staphylococci, streptococci, and pneumococci were the most frequent causal agents in their locality.

Dolenek[93] observed pseudomembranous conjunctivitis, rhinitis, and tonsillitis develop after a short catarrhal stage in a 5-month-old infant. A hemolytic Streptococcus was cultivated from the tonsils, but Pneumococcus, Moraxella lacunata (Morax-Axenfeld bacillus), and hemolytic Micrococcus pyogenes var. aureus were isolated from the conjunctiva. Rapidly progressing infiltration of the cornea led to perforation in spite of treatment.

From a study of 198 cases of conjunctivitis due to Hemophilus Aegypti (Koch-Weeks bacillus), Tanaka[94] concludes that the typical acute disease, as seen in older persons, did not occur in children. The disease was mild or asymptomatic, and children frequently were carriers and sources of epidemics. Tanaka[94] and Kućera and Dvorak[95] found streptomycin effective, whereas Ben Brahim Raïs[96] and Caruna and Hamza[97] recommended aureomycin.

89. Linnér, E.; Rickenbach, C., and Werner, H.: Comparative Measurements of Pressure in the Aqueous Veins and the Conjunctival Veins Using Different Methods, Acta ophth. **28**:469-478, 1950.

90. Trantas, N.: Cystoids Sui Generis of Bulbar Conjunctiva, Bull. Soc. héllén. opht. **18**:44-46, 1950.

91. Bocci, G.: Acquired Antibacterial Immunity of the Conjunctival Sac, Boll. ocul. **30**: 563-569, 1951.

92. Pritikin, R. I.; Duchon, M. L., and Farmer, H. S.: Bacteriology of Eye Infections in the Mid-West, U. S. Mil. Surgeon **108**:309-313, 1951.

93. Dolenek, A.: Conjunctivitis Pseudomembranacea Chronica, Československ. oftal. **7**:263-271, 1951.

94. Tanaka, C.: Studies on Conjunctivitis Caused by Hemophilus sp., Kumamoto M. J. **4**:7, 1951.

95. Kućera, K., and Dvorak, V.: Epidemic of Acute Conjunctivitis Due to Hemophilus Aegypti (Koch-Weeks Bacillus), Československ. oftal. **7**:257-262, 1951.

96. Ben Brahim Raïs: Aureomycin Treatment of Conjunctivitis Due to Weeks's Bacillus, Tunisie méd. **29**:247-249, 1951.

97. Caruna, M., and Hamza, B.: Comparative Study and Results of the Treatment of Conjunctivitis Due to Weeks's Bacillus with Antibotics, Tunisie méd. **29**:563-564, 1951.

In a study of the etiology of angular conjunctivitis, Mitsui, Himokuma, and Tanaka [98] found large diplococci, which they have tentatively called Micrococcus conjunctivae, associated with M. lacunata, in as high as 92% of the cases of diplobacillus infection.

With the use of special stains, Muscas [99] demonstrated a nucleus, which divides and later disappears from the cell, in M. lacunata. Badir [100] was unable to demonstrate inhibition of growth of the M. lacunata in cultures by sulfanilamide, sulfathiazole, or sulfadiazine. "Propamidine" (4:4'-diamidinodiphenoxypropane dihydrochloride), however, showed a strong bacteriostatic action on the organism.

Gonorrheal ophthalmia was treated by Torokhova and Tsiring [101] with drops containing 1,000 U. of penicillin per milliliter every 5 minutes the first hour, every 15 minutes the second hour, every 30 minutes the third hour, every hour thereafter for the first day, and then every 3 hours. They treated a total of 35 eyes in 21 patients—25 eyes of infants and 10 eyes of adults. Large corneal ulcers were present in seven eyes, and perforation of the cornea with prolapse of the iris was noted in four. In the newborn infant and in six of the adults gonococci disappeared from the conjunctiva within 2 to 24 hours after institution of treatment. In two eyes the organisms persisted more than 20 days, and in one of these the corneal ulcer was progressive.

Tóth [102] raises the question of the necessity of routine prophylaxis for gonorrheal ophthalmia of the newborn infant. He advises bacteriologic examination and treatment when the Gonococcus is found. However, most authors advocate some form of prophylaxis. Dolcet Buxeres [103] advises the instillation of two or three drops of a solution of sodium penicillin containing 5,000 U. per milliliter. Martius [104] treated 200 infants with two drops of an oily solution of penicillin, 100 U. per gram, immediately after birth. Wilszek,[105] using a similar preparation, treated 2,000 infants. No case of gonorrheal ophthalmia developed. However, Dolcet Buxeres [103] advises bacteriologic examination of the conjunctiva before and 24 hours and 5 days after the treatment. Gawinski [106] used drops of penicillin, 10,000 U. per milliliter. Lehrfeld [107] treated approximately 1,400 infants with penicillin ointment, 100,000 U. per

98. Mitsui, Y.; Himokuma, S., and Tanaka, C.: Etiology of Angular Conjunctivitis, Am. J. Ophth. **34**:1579-1586, 1951.

99. Muscas, M.: Existence of a Nucleus in the Diplobacillus of Morax-Axenfeld, Boll. ocul. **30**:505-512, 1951.

100. Badir, G.: Sensitivity of Morax-Axenfeld Bacillus to Sulphonamides and to Propamidine, Bull. Ophth. Soc. Egypt **41**:141-146, 1948.

101. Torokhova, L. F., and Tsiring, Z. A.: Local Therapy with Penicillin Blennorrhea of Infants and Adults, Vestnik oftal. **29**:19-21, 1950.

102. Tóth, Z.: Is Prophylaxis for Gonorrheal Ophthalmia Neonatorum Untimely and Superfluous? Klin. Monatsbl. Augenh. **118**:613-620, 1951.

103. Dolcet Buxeres, L.: Prophylaxis and Treatment of Ophthalmia of the Newborn, Arch. pediat. Barcelona **1**:145-153, 1950.

104. Martius, G.: Prophylaxis of Gonorrheal Ophthalmia with Oily Penicillin, Klin. Monatsbl. Augenh. **119**:611-619, 1951.

105. Wilszek, M.: Penicillin Prophylaxis Against Ophthalmia Neonatorum, Klin. oczna **1**:1-12, 1951.

106. Gawinski, A.: Prophylaxis and Treatment of Conjunctivitis Neonatorum, Polski tygodnik. lek. **6**:314-318, 1951.

107. Lehrfeld, L.: Penicillin Prophylaxis in Ophthalmia Neonatorum, Eye, Ear, Nose & Throat Month. **30**:367-370, 1951.

gram, without having a case of gonorrheal conjunctivitis. Davidson, Hill, and Eastman [108] treated 9,241 consecutive newborn infants with intramuscular injections of penicillin, without a failure. Equally good results were obtained by Culler and Clark [109] in 2,957 infants treated with aureomycin immediately after birth.

The incidence of blindness due to gonorrheal infection in Ohio between 1939 and 1949 was 0.4%, a value significantly lower than the 0.8% several years prior to 1939 (Freeble and Donohue [110]).

Cases of primary tuberculosis of the conjunctiva are reported by McNicolas [111] and Monbrun and Debray.[112] After being struck in the eye with a stick, a girl aged 8 years had a mammillated growth on the inner third of the upper palpebral conjunctiva associated with swelling of the lid and preauricular gland. Tubercle bacilli were demonstrated in material removed from the conjunctival mass and the preauricular gland. There was a family history of pulmonary tuberculosis. Rapid improvement and healing occurred on treatment with 0.25 gm. of streptomycin twice daily. A 15-year-old girl had a large yellowish ulcer, surrounded by congestion and edema, of the conjunctiva of the inferior temporal quadrant of the globe. This lesion was associated with a painless swelling of the preauricular gland. Tubercle bacilli were demonstrated. Complete healing followed treatment with paraaminosalicylic acid and streptomycin.

An endogenous tuberculous lesion of the conjunctiva occurring concurrently with pulmonary tuberculosis is reported by Dymitrowska [113] in a 2-year-old child.

In a series of 250 patients with phlyctenular keratoconjunctivitis Björkenheim [114] found that 98% were tuberculin-positive and 62% showed clinical signs of tuberculous infection. In the phlyctenular series antistreptolysin titers and antistaphylolysin titers were elevated in a significantly higher percentage than in a control series of patients with other external eye disease. Beta-hemolytic streptococci (Streptococcus pyogenes) and pathogenic staphylococci were recovered from throat cultures in a significantly higher percentage of the phlyctenular series than from the control series. In Alaska, Fritz and Thygeson [115] found a positive tuberculin reaction and x-ray evidence of active or inactive tuberculosis in all cases of active phlyctenulosis.

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108. Davidson, H. H.; Hill, J. H., and Eastman, N. J.: Penicillin in the Prophylaxis of Ophthalmia Neonatorum, J. A. M. A. **145**:1052-1055, 1951.

109. Culler, A. M., and Clark, S. G.: Aureomycin as Prophylaxis Against Ophthalmia Neonatorum: Second Series, Am. J. Ophth. **34**:982-984, 1951.

110. Freeble, C. R., Jr., and Donohue, J. F.: Syphilis and Gonorrhea as Causes of Blindness: A Study of Persons Declared Legally Blind in Ohio, J. A. M. A. **146**:1500-1506, 1951.

111. McNicolas, P. J.: Primary Tuberculous Complex in Conjunctiva, Irish J. M. Sc. **308**:386-387, 1951.

112. Monbrun, A., and Debray, M.: Tuberculous Primary Chancre of the Conjunctiva, Arch. franç. pédiat. **8**:162-163, 1951.

113. Dymitrowska, M.: A Case of Endogenous Tuberculosis of the Conjunctiva, Ann. Univ. Mariae Curie-Sklodowska **4**:673-679, 1949.

114. Björkenheim, B.: Precipitating Factors in Phlyctenular Kerato-Conjunctivitis: A Study on the Role of Tuberculosis and Streptococcal and Staphylococcal Infection in Phlyctenular Disease, Acta ophth., 1951, Supp. 36, p. 1.

115. Fritz, M. H., and Thygeson, P.: Phlyctenular Keratoconjunctivitis Among Alaskan Indians and Eskimos, Pub. Health Rep. **66**:934-939, 1951. Fritz, M. H.; Thygeson, P., and Dugham, D. G.: Phlyctenular Kerato-Conjunctivitis Among Alaskan Natives, Am. J. Ophth. **34**:177-184, 1951. Thygeson, P., and Fritz, M. H.: Cortisone in the Treatment of Phlyctenular Keratoconjunctivitis, ibid. **34**:357-360, 1951.

Among Eskimo children from northwestern Alaska, where the tuberculosis rate is high, these authors found twice as much active phlyctenulosis as among Indian children from southwestern Alaska, where the tuberculosis rate is relatively low. The most destructive ocular lesions were seen in children with active bone and joint tuberculosis. Although in 25 cases healing was prompt with local cortisone treatment, the authors emphasize that the disease was not cured. However, they conclude that this seemed to be the best method of aborting an acute attack. Brügger [116] reports a favorable result from treatment with 1% aureomycin ointment in a 4-year-old child, and Suster [117] obtained improvement in 4 to 10 days in 35 cases of phlyctenular keratoconjunctivitis treated with streptomycin drops or ointment. The latter author also emphasizes the necessity of general treatment.

Within two to six weeks after mass vaccination of young people in Malta with BCG, 11 children, between the ages of 4 and 8 years, had phlyctenular conjunctivitis, mostly of the limbic type. Damato [118] observed, however, that once conversion by BCG from a nonreactor to a reactor had been completed phlyctenular conjunctivitis did not appear.

Sigonnet and Cazaban [119] observed a severe case of oculoglandular tularemia which developed four days after fluid from a squashed tick from a dog had squirted into the eye. Another case with an unusual mode of infection is reported by Lindsay and Scott.[120] A man aged 40 apparently acquired the disease from contaminated sewer water.

Pletneva and Stiksova [121] found 9 cases of Parinaud's oculoglandular type of conjunctivitis in which the infective agent was probably Listera monocytogenes. Eight of the patients were between 9 and 14 years of age, and one was 36.

Newcastle disease of the conjunctiva, caused by the Tortor furens virus, was studied (Latte and Pino [122]) in human volunteers inoculated with cultures of the virus on chick-embryo allantoic fluid. After an incubation period of 12 to 24 hours, lacrimation, photophobia, itching, and dryness of the eye developed, with some edema of the lids. The conjunctiva became congested, especially at the caruncle and semilunar fold. Follicles appeared at the end of the first day and were more numerous in the lower fornix. Petechial hemorrhages developed in two patients. There was a slight discharge. The cornea was not involved. Preauricular lymphadenopathy developed in all subjects, and two patients had a slight febrile reaction. The virus was isolated from the conjunctiva during the first two or three days. Leucopenia and relative lymphocytosis developed. The formation of specific antibodies

116. Brügger, H.: Treatment of Blepharospasm and Photophobia in Phlyctenular Kerato-Conjunctivitis with a 1% Aureomycin Ointment, Tuberkulosearzt **5**:590-591, 1951.

117. Suster, J.: Personal Experiences in the Treatment of Phlyctenular Keratoconjunctivitis with Streptomycin, Československ. oftal. **7**:145-148, 1951.

118. Damato, F. J.: BCG Vaccine and Phlyctenular Kerato-Conjunctivitis, Brit. J. Ophth. **35**:416-418, 1951.

119. Sigonnet, J., and Cazaban, R.: Unilateral Oculoglandular Syndrome: Discussion of the Etiology, Tularemic Origin, Montpellier méd. **39-40**:246-247, 1951.

120. Lindsay, W. R. N., and Scott, J. W.: Oculoglandular Tularemia Transmitted from Contaminated Sewer Water, Canad. J. Pub. Health **42**:146-151, 1951.

121. Pletneva, N. A., and Stiksova, V. N.: Oculoglandular Form of Listerellosis, Vestnik oftal. **29**:17-21, 1950.

122. Latte, B., and Pino, G.: Experimental Infection of the Human Conjunctiva in Volunteers by the Virus of Newcastle Disease, Boll. ocul. **30**:553-562, 1951.

was inconstant, and reinoculation of two subjects resulted in milder signs and symptoms. Treatment with aureomycin was ineffective.

Radnot [123] records four cases of Newcastle disease in which the virus was demonstrated, and a very similar infection of the human conjunctiva is described by Borsello and Mantovani,[124] from which the Italian pseudopest virus was isolated.

From histologic studies Capolongo [125] concludes that some of the nodular and vesicular lesions of the conjunctiva in smallpox are allergic.

Teng [126] attributed vaccinial keratitis in a 4-month-old infant to accidental inoculation, even though the clinical description did not exclude the possibility of vascular dissemination of the virus.

Gangosa, a particularly severe manifestation of tertiary frambesia causing destruction of the eyelids, was observed in the Belgian Congo by Habig.[127]

Rebello Machado [128] and Fazakas [129] warned that any sluggish refractory process in the external membranes of the eye should be suspected of possible mycotic origin. Infections of the lids, lashes, brows, conjunctiva, cornea, eyeball, lacrimal apparatus, and orbits have occurred. The following genera have been reported with some frequency. Trichophyton, Sporotrichum, Actinomyces, Rhinosporidium, Blastomyces, Penicillium, and Aspergillus. Theodorides and Koutrolikos [130] add a case of blastomycosis of the conjunctiva.

The first case of infestation of the conjunctival sac with larvae of Oestrus ovis to occur in England is reported by Smith.[131] Kornilova [132] found 11 larvae in the conjunctival sac of one of his patients and 8 larvae in another.

Ophthalmomyiasis due to Dermatobia cyaniventris was encountered in 77 patients by Velloso Vianna,[133] who describes an original forceps for removal of the larvae.

An unusual type of conjunctivitis which occurred in 50 patients in Denmark is reported by Kall,[134] who found formations resembling protozoa of the Leucocytozoon-Haemoproteus group in the epithelial and subepithelial layers.

123. Radnot, M.: A Viral Disease of the Eye, Ophthalmologica **121**:287-289, 1951.

124. Borsello, G., and Mantovani, G.: Conjunctivitis Due to an Accidental Infection of Italian Pseudopest Virus of Fowls in Man, Rass. ital. ottal. **19**:452-457, 1950.

125. Capolongo, G.: Histological and Pathogenic Investigations on Conjunctival Nodules and Vesicopustules in Smallpox, Arch. ottal. **54**:135-150, 1950.

126. Teng, C. A.: Vaccinia with Ocular Involvement: A Case Report, Chinese M. J. **69**:58-59, 1951.

127. Habig, J. M.: Conjunctival Metaplasia and Pigmentation in Frambesia, Bull. Soc. belge opht. **95**:468-473, 1950.

128. Rebello Machado, N.: Infections of the Eye Caused by Fungi, An. Soc. mexicana oftal. **24**:61-95, 1950.

129. Fazakas, S.: Report on Oculomycoses Due to the Fungous Flora of Human Eyes, Ophthalmologica **121**:249-258, 1951.

130. Theodorides, E., and Koutrolikos, V.: Blastomycosis of the Conjunctiva, Bull. Soc. héllén. opht. **18**:107-112, 1950; Am. J. Ophth. **34**:535-538, 1950.

131. Smith, R.: Ophthalmomyiasis in England, Brit. J. Ophth., **35**:242-243, 1951.

132. Kornilova, A. F.: Two Cases of Larvae of Botflies in the Conjunctival Sac, Vestnik oftal. **29**:41-42, 1950.

133. Velloso Vianna, E.: Ophthalmomyiasis Due to Dermatobia Cyaniventris: Treatment, Arch. brasil. oftal. **14**:47-54, 1951.

134. Kall, E.: Conjunctivitis of Possible Protozoal Origin Occurring in Denmark, Acta ophth. **28**:409-420, 1950.

A small vascular limbic tumor, 1 cm. in diameter, in a 9-year-old boy was diagnosed as bilharzial granuloma by biopsy (Izz El Din Naim [135]). Urinalysis revealed ova of Bilharzia (Schistosoma) haematobium.

A child from the Belgian Congo is reported by de Coster and Rodhain [136] to have harbored two Porocephalus nymphs in subconjunctival cysts for 12 months, without either pain or inflammation.

According to Tóth,[137] two patients with lymphatic keratoconjunctivitis failed to respond to treatment until intestinal parasites, Oxyuris and Taenia nana, were eliminated.

Costi [138] calls attention to the frequent occurrence of a form of subacute conjunctivitis, characterized by hyperemia and marked dilatation of the conjunctival vessels, smarting photophobia, marked prurigo, and slight secretion, which proves resistant to all forms of antiseptic treatment. Bearing in mind the possible allergic nature of the disease, the author gave general antiallergic medical treatment, without important results. However, desensitizing treatment with especially prepared autogenous vaccines produced remarkably satisfactory results.

Bocci [139] reports the successful production of local anaphylactic phenomena in the conjunctiva of rabbits with bacterial antigens. Staphylococcus vaccine or antitoxin was instilled into one eye of rabbits twice a day for eight days. One month later intense hyperemia and abundant secretion developed in the treated eye 12 hours after the intravenous injection of the antigens. Urayama,[140] in a somewhat similar series of experiments, used application of heat and cold instead of antigens to one eye and concluded that a hypersensitivity, or allergic hypergia, could be fixed to the eye by means of nonspecific stimulation even when antigenic substances were not administered locally.

Sherman and Feldman [141] found that intramucosal tests could be made in clinical allergies when the reactions to skin tests were negative. They made a tiny bleb on the bulbar conjunctiva just below the cornea by injecting 0.02 ml. of the test material. A positive reaction, consisting of engorgement of the vessels, reached its height in 10 minutes and began to subside in 20 to 30 minutes. The authors advise against the routine use of this test.

D'Ermo and Salvi [142] tested the action of the synthetic antihistaminics on the bacterial flora of the conjunctiva. They found that all the drugs had some antibacterial effect but that the action was weak.

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135. Izz El Din Naim, A.: Bilharzial Limbal Tumour, Bull. Ophth. Soc. Egypt **41**:99-101, 1948.

136. de Coster, P., and Rodhain, J.: Ocular Localization of Porocephalus Nymphs in a Native Child, Ann. Soc. belge med. trop. **31**:331-335, 1951.

137. Tóth, Z.: Symptoms of Keratoconjunctivitis Lymphatica in Helminthiasis, Klin. Monatsbl. Augenh. **119**:16-19, 1951.

138. Costi, C.: A Certain Variety of Allergic Conjunctivitis, Bol. Inst. patol. med. Madrid **6**:7-8, 1951.

139. Bocci, G.: Ocular Anaphylaxis Against Bacterial Antigens, Boll. ocul. **30**:433-442, 1951.

140. Urayama, A.: Experimental Study on Fixation of Allergic Reaction to the Eye, Tohoku J. Exper. Med. **53**:207-215, 1951.

141. Sherman, H., and Feldman, L. A.: Intramucosal Test and a Comparison of Its Reactivity with the Intradermal and Conjunctival Reactions, Ann. Allergy **8**:734-739, 1950.

142. d'Ermo, F., and Salvi, G. L.: Antihistaminics and the Eye: IV. Action in Vitro of Some Antihistaminics on Bacteria of the Conjunctiva, Boll. ocul. **30**:3-11, 1951.

Fronimopoulos [143] reports that an ointment of 0.035% berberine and 0.035% hydrastine sometimes was effective in patients with hypersensitive conjunctivas when cocaine, epinephrine, and other ointments had failed.

Drawing on a long period of clinical and histologic research, Pascheff [144] concludes that vernal conjunctivitis exhibits three periods of evolution: (1) infiltrative; (2) hyperplastic, and (3) regressive-degenerative. He considers the disease an allergic conjunctivitis which depends externally upon the solar heat rays and internally upon an infectious lymphatic adenopathy. However, Rossi [145] emphasizes the frequency with which the disease occurs in young persons with endocrine disorders.

Morpurgo [146] reports two cases of vernal conjunctivitis with concomitant corneal lesions consisting of epithelial and parenchymal opacities with vascular proliferation. He considers that these lesions are due partly to disturbances in corneal nutrition and partly to an extension of the limbic changes into the cornea.

Eriksen [147] successfully treated one patient with typical vernal conjunctivitis by desensitization to cow's epithelium after a positive intracutaneous test. Dededimos [148] found that cauterization of the sphenopalatine ganglion reduced the subjective discomforts and caused a decrease in the limbic vegetations. Nano,[149] on the other hand, reports prompt improvement with the use of cortisone drops every two hours. Treatment was continued until all symptoms had disappeared, usually 8 to 30 days, and beneficial results were maintained for a considerable period.

Cadle and Magill [150] determined that the ocular irritation produced by "smog" in Los Angeles was due to a mixture of atmospheric contaminants. Gaseous parts of the mixture were more irritating than ozone and gasoline products.

Nemec [151] treated 25 patients with conjunctival injury and staining from copying pencils by irrigation with saline and local anesthesia of the conjunctiva, followed by the subconjunctival injection of 1 ml. of ascorbic acid with a small amount of procaine hydrochloride. The ascorbic acid promptly neutralized and decolorized the basic dye.

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143. Fronimopoulos, J.: Action of Berberine and Hydrastine on Eyes, Tr. Greek Ophth. Soc. **18**:459-462, 1950.

144. Pascheff, C.: Vernal Conjunctivitis in Bulgaria, Bulgarska Akad. naukite **149**:1-91, 1951.

145. Rossi, A.: Vernal Conjunctivitis: Etiology and Treatment, Rass. ital. ottal. **20**:48-58, 1951.

146. Morpurgo, F.: Corneal Changes in Vernal Conjunctivitis, Gior. ital. oftal. **4**:295-302, 1951.

147. Eriksen, A.: An Allergic Conditioned Case of Conjunctivitis Vernalis, Acta ophth. **29**:91-94, 1951.

148. Dededimos, P.: Sympathetic Origin of Spring Catarrh and Allergic Conjunctivitis, Bull. Soc. héllén. opht. **18**:216-223, 1950.

149. Nano, H. M.: Treatment of Vernal Conjunctivitis with Cortisone, Rev. Asoc. méd. argent. **64**:585-587, 1950.

150. Cadle, R. D., and Magill, P. L.: Study of Eye Irritation Caused by Los Angeles Smog, A. M. A. Arch. Indust. Hyg. **4**:74-84, 1951.

151. Nemec, H.: A New Treatment of Basic Eye Burns (Copying Ink Pencils), Klin. Monatsbl. Augenh. **119**:540-542, 1951.

In cases of ocular burns, Nagy [152] advises the instillation of 10% benzazoline (priscol®) hydrochloride hourly for the first four or five days if there is no indication for immediate grafting. The treatment gave satisfactory results in 30 cases.

Cruthirds,[153] Pandit,[154] and Kuhn [155] draw attention to the role of sulfhydryl preparations in tissue protection and repair. They used "hydrosulphosol" (calsulfhydryl) in the treatment of various chemical, thermal, and ultraviolet burns of the eye.

Spinning-mill keratoconjunctivitis in the viscose rayon industry appeared only after two to four consecutive days of working in a spinning room. Masure [156] found that the incidence varied according to the concentration of hydrogen sulfide in the air, although predisposition played an unquestionable, but unexplained, part. The lesions were reproduced in animals with hydrogen sulfide and with a mixture of hydrogen sulfide and carbon disulfide gas. Vasoconstrictors, such as naphazoline, afforded relief but did not modify the course of the disease, whereas benzazoline seemed to shorten the duration.

A thorough review of the ocular complications of erythema exudativum multiforme and their treatment was made by Duggan and Gaines,[157] and new cases were described by Pereyra [158] and Crawford and Luikart.[159]

Badir [160] describes a case of Behcet's syndrome (recurrent iritis with hypopyon, aphthous ulcers of the buccopharyngeal mucosa, and ulcers on the genitalia) and concludes by suggesting a new line of treatment, i. e., desensitization with staphylococcus toxoid.

In the course of 10 years, Nyfos [161] observed seven patients with Reiter's syndrome (polyarthritis, urethritis, and conjunctivitis), in all of whom the disease showed a pronounced tendency to recur but ran a benign course. De Moura's [162] patient improved rapidly on small doses of neoarsphenamine.

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152. Nagy, F.: Treatment of Ocular Corrosions and Lesions Due to Burns with Priscol,® Ophthalmologica **121**:345-352, 1951.

153. Cruthirds, A. E.: Sulfhydryl Therapy in Ophthalmology: Progress Report, Ann. West. Med. & Surg. **5**:554-557, 1951; Sulfhydryl in Tissue Respiration and Repair as Applied to Burns in Ophthalmology, J. Internat. Coll. Surgeons **16**:356-364, 1951.

154. Pandit, Y. K. C.: Hydrosulphosol in Treatment of Burns and Injuries of the Cornea, Indian J. Med. Sc. **5**:34-39, 1951.

155. Kuhn, H. S.: Chemical Eye Injuries and Ophthalmic Hydrosulphosol, Tr. Am. Acad. Ophth. **55**:749-752 (Sept.-Oct.) 1951.

156. Masure, R.: Spinning-Mill Keratoconjunctivitis in the Vicose Rayon Industry, Rev. belge path. et méd. exper. **20**:297-341, 1951.

157. Duggan, J. W., and Gaines, S. R.: Ocular Complications of Erythema Exudativum Multiforme, Am. J. Ophth. **34**:189-197, 1951.

158. Pereyra, L.: Syndrome of Stevens-Johnson: Relations with Polymorphic Erythema and Pemphigus; Clinical and Histopathologic Contribution, Gior. ital. oftal. **4**:132-149, 1951.

159. Crawford, G. M., and Luikart, R. H.: Severe Erythema Multiforme with Intestinal Involvement, J. A. M. A. **140**:780-781, 1949.

160. Badir, G.: Behcet's Syndrome with Description of a Case, Bull. Ophth. Soc. Egypt **41**:119-129, 1948.

161. Nyfos, L.: Reiter's Syndrome, Nord. med. **46**:1868-1871, 1951.

162. de Moura, A.: Reiter's Syndrome: A Case with Favorable Reaction to 914 (Neoarsphenamine), Rev. port. obst. ginec. e cir. **4**:70-76, 1951.

A peculiar type of hypertrophic conjunctivitis which occurred in 202 of 2,184 students on the Isle of Margarita (Lesser Antilles) is described by Grom [163] as being intermediate in type between follicular conjunctivitis and beginning trachoma. The cause was not determined. Another, and rarer, type of hypertrophic conjunctivitis is described in two cases by Pascheff.[164]

Forster [165] compared the value of Schirmer's test and that of rose-bengal staining of the conjunctiva in the diagnosis of keratoconjunctivitis sicca in a series of 98 eyes and concluded that the dye test was more accurate. Sjögren [166] warns that the instillation of a local anesthetic before applying the dye to the conjunctiva has given a picture similar to that of the sicca syndrome, and that therefore local anesthetics must not be used in making the test. Additional cases of the disease are reported by Poli and Wiel [167]; Schachter and Ourgaud,[168] and Lackington, Charlin, and Gormaz.[169]

Localized injection of the upper quadrant of the bulbar conjunctiva, either monocularly or binocularly, associated with symptoms of irritation were found by deRoetth [170] to be associated with infections elsewhere in the body. Five cases of this type are reported. When the distant infection was eliminated, the eye improved.

Pemphigoid shrinkage of the conjunctiva with epidermoid transformation of the mucosa and epidermal overgrowth, producing total occlusion of the puncta, were the ocular complications described by Frandsen [171] in a case of familial poikiloderma atrophicans vasculare in a man aged 40.

Diffuse hyperplasia, which eventually developed into a circumscribed swelling in various types of conjunctivitis, is listed by Pascheff [172] as follows: hyperplasia of plasma cells, resulting in plasmoma or plasmocytoma; confluence of follicles in trachoma, producing folliculoma; papillofibromata in vernal conjunctivitis, and hyalinoma in trachoma. A benign epibulbar lymphoma of this type is reported by Enroth [173] in a man aged 49 and Anastasi [174] describes unilateral nodular epithelial

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170. de Roetth, A., Sr.: Localized Injection of the Upper Quadrant of the Bulbar Conjunctiva, A. M. A. Arch. Ophth. **46**:560-564, 1951.

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hyperplasia of the conjunctiva and cornea in a patient aged 72. Microscopic examination revealed epithelial hyperplasia associated with metaplastic and degenerative lesions.

Two cases of prickle-cell epithelioma of the conjunctiva are reported by Grom.[175] One is that of a woman aged 27, and the other, that of a 10-year-old child with xeroderma pigmentosum.

A yellowish, well-defined, thin tumor, 5 by 3.5 mm., located at the inferior nasal limbus, was found to be an adenoma with histologic structure almost identical with that of the lacrimal gland (François and Rabaey[176]).

A case of congenital melanosis of the bulbar conjunctiva found in a woman aged 55 is described by Tsopelas and Vartzelis.[177] Two cases of nevus pigmentosus were studied histologically by Zanen and Brihaye-van Geertruyden[178] in an attempt to define the first signs of malignancy, which they conclude are loss of cohesion of the epidermal cells where the epithelial lacunae are formed, corresponding with the extension of the tumor.

Friede[179] discusses the poor surgical results following the development of total symblepharon in chronic pemphigus and recommends surgical intervention at the beginning, when the conjunctival sac begins to shrink. He advises that the conjunctiva be incised in both fornices and the episclera excised. A tape-like implant of mucous membrane of the lip should then be sutured to the previously cauterized sclera.

Putshkovskaya[180] found that shortening of the fornices would follow the repair of complete symblepharon unless the mucous-membrane graft was sutured to the episclera. Two sutures were placed on each side of the rectus tendon. In 10 of 13 eyes with extensive symblepharon a single operation produced satisfactory results. In four eyes with complete symblepharon of both lids the results were good, and in four there was moderate improvement.

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176. François, J., and Rabaey, M.: Adenoma of the Limbal Conjunctiva, Brit. J. Ophth. **35**:237-241, 1951; Adenoma of the Limbal Conjunctiva, Bull. Soc. belge opht. **96**:549-556, 1950.

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News and Comment

EDITED BY DR. W. L. BENEDICT

KARL LINDNER, M.D.

A Birthday Message

WHEN I offered to submit a few remarks to the Editor of the ARCHIVES about Prof. Karl Lindner, whose seventieth birthday the ophthalmological world has good cause to celebrate this January, I was delighted that, as one of his oldest American friends, the opportunity was granted me.

Karl Lindner was born in Vienna on Jan. 19, 1883. He attended the Medical School at the University of Vienna, studied in Paris in the winter of 1905-1906, and took his degree in Vienna in 1907. His ophthalmological training was obtained at the eye clinic of Prof. Ernst Fuchs. He was granted the Welz-Graefe award for 1911 to 1913 by the German Ophthalmological Society in Heidelberg for fundamental investigations on trachoma. In 1916 he assumed the duties of a university lecturer in ophthalmology at the University of Vienna. He was at that time Professor Fuchs's assistant and after Professor Fuchs's retirement became Dr. Dimmer's assistant. In 1924 he was in charge of the ophthalmological section at the Poliklinik in Vienna and in that year also was appointed associate professor. He succeeded Professor Dimmer as director of the Second University Eye Clinic in 1927, with the title of professor in 1928. For the year 1948-1949 he was dean of the Medical School.

Professor Lindner is a member of the Vienna Ophthalmological Society, the German Ophthalmological Society, and the Gesellschaft der Aerzte in Vienna. His scientific papers are concerned with many phases of ophthalmology. In addition to the monograph entitled "The Determination of Astigmatism by Means of Retinoscopy with Cylinders" (1927) and the chapters on trachoma in both editions of Berens' textbook, "The Eye and Its Diseases," he has published 115 scientific articles. Deserving of special mention are his basic studies dealing both with trachoma and with the topography of the micro-organisms of the conjunctiva, and a series of publications on the determination of astigmatism by means of retinoscopy with cylinders and by means of such subjective methods as velonoskiascopy and the use of crossed cylinders. Another series of important papers are those dealing with the pathogenesis and treatment of retinal detachment, the elaboration of the Leber-Gonin theory of the development of retinal tears, and the introduction of the *Lochbrille*, the demarcation method, the undermining operation, and the scleral resection. In further publications, Lindner advanced our knowledge of the clinical pathology of the vitreous body and improved the technique of cataract extraction. Additional contributions to surgery are contained in articles on the operative treatment of injuries to the lids, on muscle surgery, on operations for glaucoma and ptosis, on the extraction of intraocular foreign bodies, and on keratoplasty. More recent publications have dealt with the pathology of myopia. In 1952 Professor Lindner's "Lehrbuch der Augenheil Kunde" appeared. It embodies the result of his extensive scientific achievements, his manner of representation expressing his experience as a great teacher.

In the introduction of his textbook, he states: "I have never before found the time to write a textbook, for I was always busy trying to find answers to new problems." In this sentence he epitomizes his life as a scientist in ophthalmology; indefatigability, an inquisitive mind, sharp logic, and the facility of clearly demonstrating his thoughts to students and colleagues have been, and still are, his main characteristics. Occasionally, when a hypothesis cannot be proved but always works in practice, he says in explanation: "But I tell you, it is so!" There is a definite Viennese witticism in that remark, for he is a great clinician, in addition to being

Dr. Karl Lindner

a scientist. Clinically the proof is that the thing works. Over a period of these many years, with immense material at his disposal, and starting his career as the youngest assistant of that unequaled genius in ophthalmology Ernst Fuchs, he has accumulated and digested a treasure of clinical wisdom that few men have been able to equal. The constant teaching not only of Viennese students, but also of a great number of foreigners, especially Americans, as in the courses he gave in Vienna through arrangement with the American Medical Association, not only enriched his listeners but always kept him abreast with the newest development in ophthalmology, as did his frequent visits to other countries, including the United States.

It must not be forgotten that this great quantity of work—laboratory investigations, clinical care of a large material, numerous teaching hours, the duties of an executive, and private practice took place during years such as his native city and his country had never before experienced. The end of World War I saw the end of the Hapsburg Empire. Austria was shrunken to a small strip. For years almost unbelievable inflation existed. People lost everything they had. The clinic and hospital were without heat, without supplies, with dull instruments, and with insufficient help. No sooner had the city and country recovered from this catastrophe than a second world war swept away all that had been accomplished and struck again at the roots of all peace and prosperity, with, finally, occupation of the city by the enemy. It is one thing to accomplish what Professor Lindner did in peace and quiet, and an entirely different thing to accomplish it in times of such distress, finally taking care of his patients personally day and night in the basement of the Krankenhaus while bullets were flying in the streets, and in spite of tragic personal losses, Lindner never stopped working and never lost his firm Protestant faith and courage or his sense of humor.

His career began with no advantages; his finances were limited; no political or social efforts were made by him or in his behalf; his modesty and simple way of living characterized him then, as they do now. His pleasures have always been simple, and his family life, like his friendships, close and intimate.

On his seventieth birthday, then, his many friends and students in the United States send him their cordial good wishes and congratulations, with the hope that the years beyond the Biblical threescore and ten will be his, in peace, quiet, and happiness with his family, and still good work to be done. May his bees continue to gather honey and his fruit trees blossom in the spring!

HANS BARKAN, M.D.

GENERAL NEWS

Formal dedication of the Department of Research Laboratories of the Wills Eye Hospital took place at the hospital on Tuesday, Oct. 7, at 2 p. m. The three-story colonial structure, which is fully equipped for ophthalmic research, is located directly behind the hospital.

The administrative and medical staffs of Wills Eye Hospital feel that this occasion initiated the outstanding event of ophthalmological significance in a long time.

Ernest T. Trigg, vice-president of the Board of Directors of City Trusts, and chairman, Committee on Wills Eye Hospital, presided at the dedication ceremony. Rt. Rev. Oliver J. Hart, D.D., Episcopal Bishop, Diocese of Pennsylvania, pronounced the invocation. The principal address was delivered by former Associate Justice of the United States Supreme Court, Owen J. Roberts.

Other brief addresses were given by John A. Diemand, president, Board of Directors of City Trusts; Michael J. Byrne, deputy to the Mayor of Philadelphia; Dr. Edmund B. Spaeth, president, the hospital's Board of Attending Surgeons; Dr. Irving H. Leopold, director, Department of Research, and William C. Brown, secretary, Pennsylvania State Department of Welfare.

Approximately 300 persons, including city and state officials, attended the event, which marked a milestone of achievement in the long history of the Wills Eye Hospital, which, since its establishment in 1832, has been dedicated solely to the prevention of blindness.

Call for Papers for the Annual Meeting, Section on Ophthalmology, American Medical Association.—The Annual Meeting of the Section on Ophthalmology of the American Medical Association will be held jointly with the Association for Research in Ophthalmology, Inc., in New York during the first week in June, 1953. The Scientific Exhibit of the Annual Session of the American Medical Association will run concurrently at the Grand Central Palace.

Titles and full abstracts of papers submitted for presentation at the meetings of the Section should be in the hands of the Secretary, Dr. Trygve Gundersen, not later than Jan. 1, 1953. This is necessary for the proper selection of papers and for the necessary arrangements for their competent discussion.

Papers of a technical nature are better submitted to the Association for Research in Ophthalmology. The winter sectional meeting of the Association will be held this year in Baltimore. Early submission of material is prerequisite for its inclusion in the program.

The Scientific Exhibit will entertain presentations of a purely ophthalmological nature, but would prefer to have material of interest also to the general practitioner. An exhibit in conjunction with a paper read before the section is of particular interest. The material can be either of a research or of an instructional nature.

Inquiries may be addressed to Dr. Henry F. Allen, of the Program Committee of the Section, or to one of the following:

Section on Ophthalmology:—

Trygve Gundersen, M.D.
101 Bay State Rd.
Boston 15

Association for Research in Ophthalmology:—

Hunter H. Romaine, M.D.
111 East 65th St.
New York 21

Scientific Exhibit:—

William F. Hughes Jr., M.D.
1853 W. Polk St.
Chicago 12

It is hoped that a lively response to this opportunity will be forthcoming.

Eighteenth International Congress of Otoneuro-Ophthalmology.—The Eighteenth International Congress of Otoneuro-Ophthalmology will be held in Bologna, Italy, from May 3 to 7, 1953; chairman, Prof. Q. di Marzio. The official program is as follows:

	Reporters
I. Dysraphia in Otoneuro-Ophthalmology	
Embryology	Krabbe (Copenhagen)
Neurology	Vercelli (Milan)
Radioneurology	Mascherpa (Milan)
Otolaryngology	Arslan (Padua)
Ophthalmology	Franceschetti (Geneva)
Neurosurgery	Fasiani (Milan)
Facial Surgery	Sanvenero-Rosselli (Milan)
General reporter	Belloni (Padua)
II. Ménière's Disease	
Neurology	Barré (Strasbourg)
Otology	Greiner (Strasbourg)
Neurosurgery	Tolosa (Barcelona)

The official languages are Italian, English, German, French, and Spanish.

Besides the papers on topics indicated above, papers will be accepted discussing at least two specialties at the same time.

Colleagues interested in attending the Congress are requested to send their names and addresses immediately, so that they may be sent a provisional program, in which they will find all information on registration, facilities at their disposal, and transportation.

Anyone who wishes to submit a paper or to take part in the discussions should apply to the General Secretary, Dr. Giuseppe Cristini, Clinica Oculistica, Policlinico, Bologna, Italy.

Symposium on Retinal Diseases, State University of Iowa College of Medicine.—A symposium on retinal diseases, under the sponsorship of the Department of Ophthalmology, University of Iowa College of Medicine, will be held in Room 105 of the University Hospital on March 30 and 31, 1953. The following subjects will be presented:

Molecular Basis of Visual Excitation, Dr. George Wald; Hypertension and Changes in the Fundus of the Eye, Dr. Herman Elwyn; Clinical Evaluation of Spasm in Hypertensive Retinopathies and in Vascular Occlusions, Dr. Henry P. Wagener; Diabetic Retinopathy, Dr. Jonas S. Friedenwald; Etiology and Classification of Retinal Detachment, Dr. C. L. Schepens; Pathology of Retinal Detachment, Dr. Dohrmann K. Pischel.

Registration is open to ophthalmologists. The fee is $50.

Applications should be sent, with fee, to the Director of Postgraduate Studies, Room 259, Medical Laboratories Building, Iowa City.

PERSONAL NEWS

Plans to Honor Dr. Lawrence T. Post.—The staff of the Department of Ophthalmology, Washington University School of Medicine, Saint Louis, have completed plans for the recognition of the retirement, as head of the department, of Dr. Lawrence T. Post, who for the past twenty years has held that position.

On Saturday, March 28, 1953, during the day a scientific session will be held, the contributors being Dr. Post's friends and confreres in American ophthalmology. These speakers include Drs. James H. Allen, Walter S. Atkinson, Alson E. Braley, Paul Chandler, Frederick C. Cordes, Jonas S. Friedenwald, Everett L. Goar, A. Ray Irvine, Peter Kronfeld, Donald J. Lyle, William P. McGuire, A. D. Ruedemann, and Alan C. Woods. That evening a testimonial dinner will be held at the Park Plaza Hotel, honoring Dr. Post.

On the preceding day, March 27, 1953, the Midwestern Section of the Association for Research in Ophthalmology, Inc., will hold its annual scientific session at the Washington University School of Medicine. Also, on the night of March 27 the Saint Louis Ophthalmic Society will have Dr. Lawrence T. Post as its honor guest, and he will deliver the paper of the evening.

All those who are interested are cordially invited to attend either the scientific session or the dinner or both. Those planning to attend the dinner are requested to make reservations well in advance through the departmental secretary, Department of Ophthalmology, Washington University School of Medicine, 640 S. Kingshighway Blvd., Saint Louis 10.

SOCIETY NEWS

Midwestern Section of Association for Research in Ophthalmology, Inc.—The Fifth Annual Meeting of the Midwestern Section of the Association for Research in Ophthalmology, Inc., will be held at the Oscar Johnson Institute, Elliot Auditorium, 640 South Kingshighway, St. Louis, on March 27, 1953, begin-

ning at 9:00 a. m. The Midwestern Section encompasses the states of Colorado, Illinois, Indiana, Iowa, Kansas, Minnesota, Missouri, Nebraska, North and South Dakota, and Wisconsin.

Ophthalmological Society of Egypt.—The Ophthalmological Society of Egypt will celebrate its fiftieth anniversary during its annual general meeting, to be held in Cairo, in the latter half of February, 1953. Guests of the Society will include Dr. David G. Cogan, Boston; Prof. Dr. Karl Lindner, Vienna, Austria; Mr. Keith Lyle, London, England; Prof. Dr. Louis Paufique, Lyons, France; Prof. Dr. R. Theil, Frankfurt, Germany, and Prof. Dr. P. Thygeson, San Jose, Calif.

Dr. Mohammad Khalil, 15A Sherif Pasha St., is secretary of the Society.

Irish Ophthalmological Society.—The annual meeting of the Irish Ophthalmological Society will be held in the Royal Victoria Eye and Ear Hospital, Dublin, on April 16 and 17, 1953.

Books

Advances in Ophthalmology. Edited by E. B. Streiff. Price, 39.50 Swiss francs. Pp. 291. S. Karger, Ltd., Holbeinstrasse 22, Basel; 215 4th Ave., New York, 1952.

This new publication takes the place of the review articles which formerly appeared in *Ophthalmologica*. These were copied after the type of review formerly published in the old *Zeitschrift für Augenheilkunde*. Each subject is to be reviewed by a competent collaborator every three to five years. The articles are published in English, German, or French. In the present volume the following subjects are reviewed:

Treatment of Concomitant Strabismus	T. Keith Lyle	English
History of Ophthalmology	G. ten Doesschate	English
Methods of Investigation	H. M. Dekking	English
Optic Nerve and Chiasm	von A. Biemond	German
Crystalline Lens	J. Nordmann	French
Cataract Surgery	C. Heydacker	French
Glaucoma	von G. Goldmann	German

This volume is unquestionably valuable, as one may judge by the imposing list of contributors. The book will have serious competition, however, in English-speaking countries, from several reviews which have recently appeared in English.

Transactions of the International Optical Congress, 1951. Sponsored by the British Optical Association. Price, £2.12. Pp. 493, with numerous illustrations. British Optical Association, 65 Brook St., London, W. 1, 1952.

This, the first International Optical Congress, was held in Kings College, London, from July 9 until July 13, 1951. There were 800 registrations received from 24 countries, including the United States. The papers cover a wide variety of subjects, including the ophthalmoscope, physiological optics, accommodation and convergence, binocular vision and stereopsis, refraction, orthoptics, and contact lenses, with a few papers on general subjects, such as vision and the vehicle driver, and the etiology of migraine.

The British Optical Association Foundation Lecture was delivered by Mr. J. Z. Young, on "Visual Perception in Relation to Speech." The papers range enormously in intellectual level, as would be expected. For example, a paper on the clinical uses of the ophthalmoscope would be suited to the student beginning his course in ophthalmology. On the other hand, a paper such as "The Significance of Luneberg's Contribution to Physiological Optics" requires a knowledge of optics which only few ophthalmologists in this country possess.

The volume is worth perusing with a critical eye.

Studies in Visual Optics. By Joseph I. Pascal, M.D. Price, $12.50. Pp. 800, with 138 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1952.

The author of this new text in optics has had a wide experience in teaching optics. In this book he collects the many contributions he has made and presents the usual material from a fresh point of view. Not all his observations and recommendations will be agreed to, but they are all stimulating and help to point up how little we really know about some very elementary subjects with which we are constantly dealing.

The book is well printed and adequately illustrated. It is recommended for those who already have sufficient knowledge of optics to weigh for themselves some of the controversial issues.

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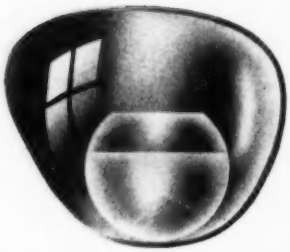

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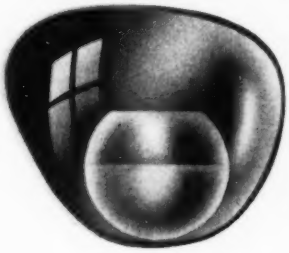

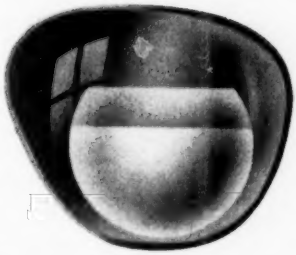

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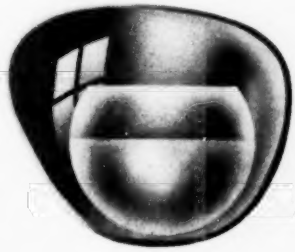

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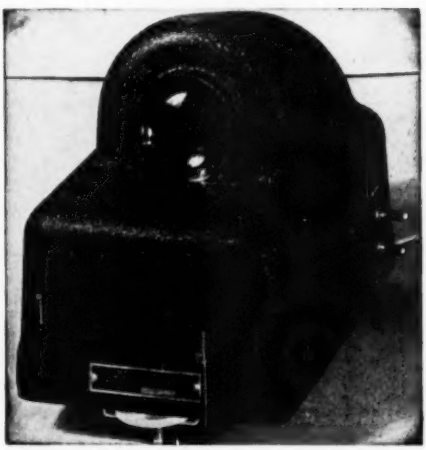

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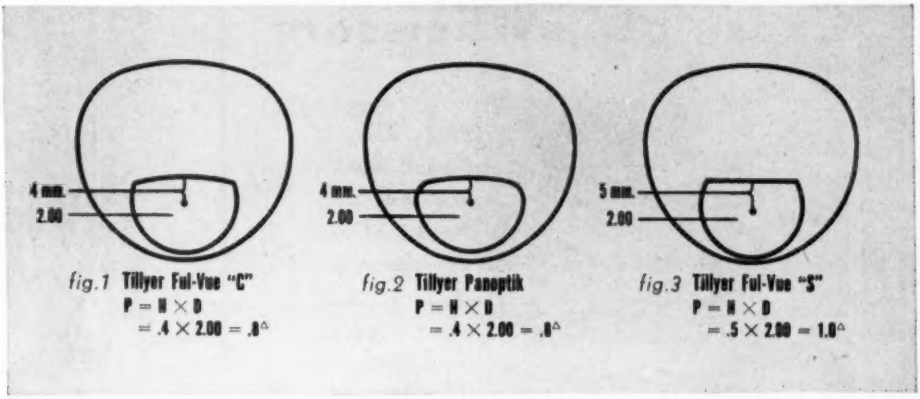

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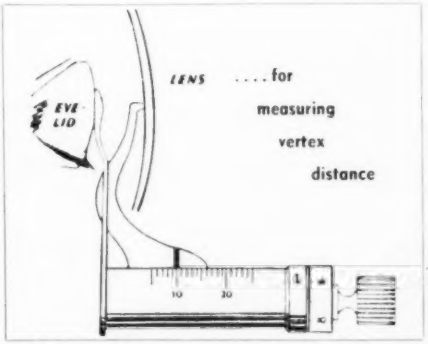

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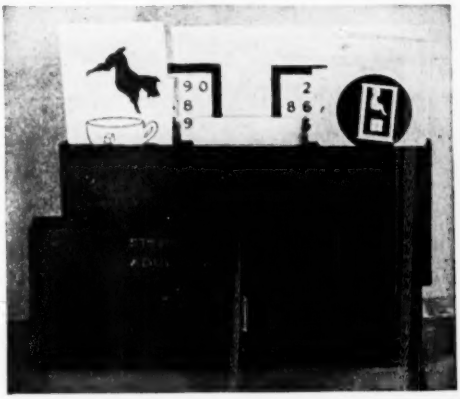

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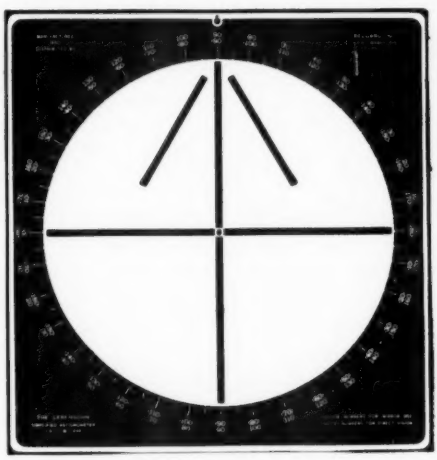

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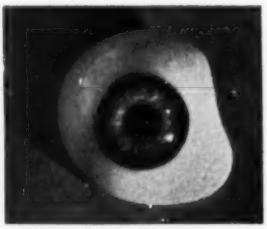

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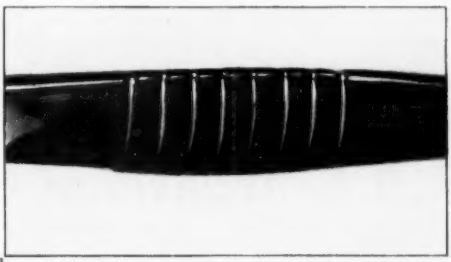

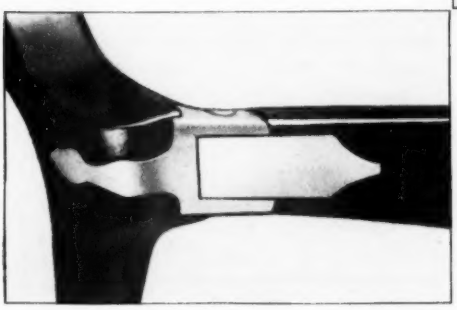

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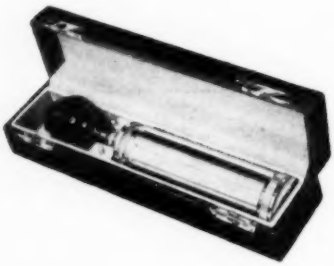

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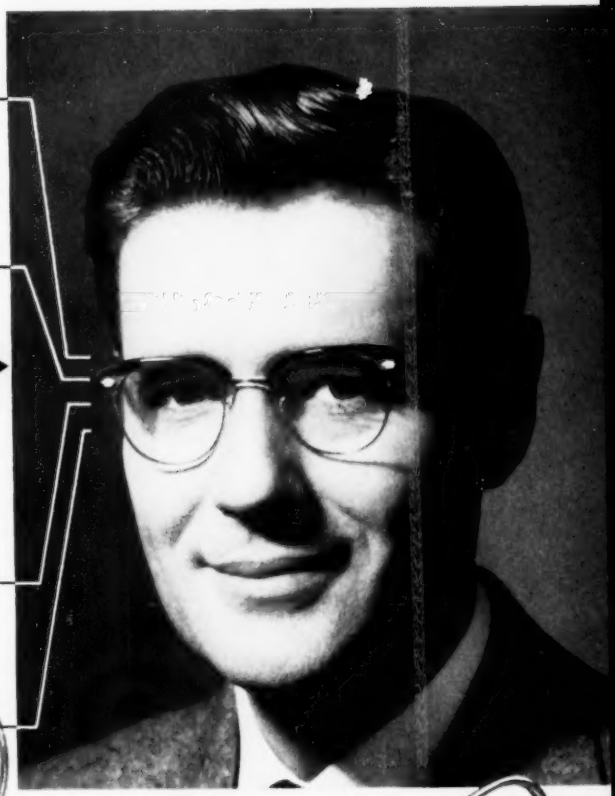

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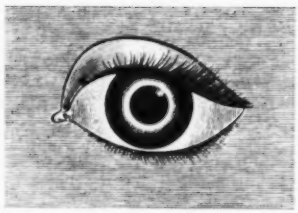

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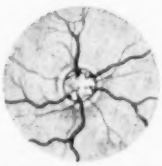

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